

Figure 1.

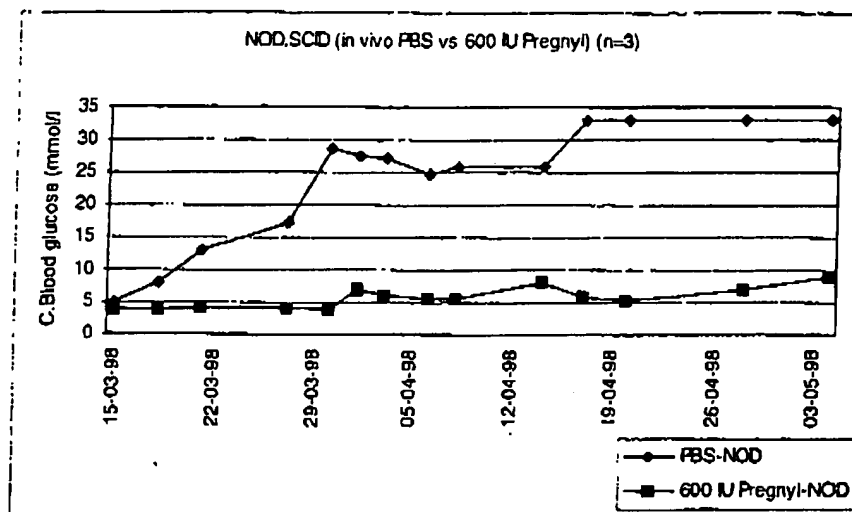


Figure 2.

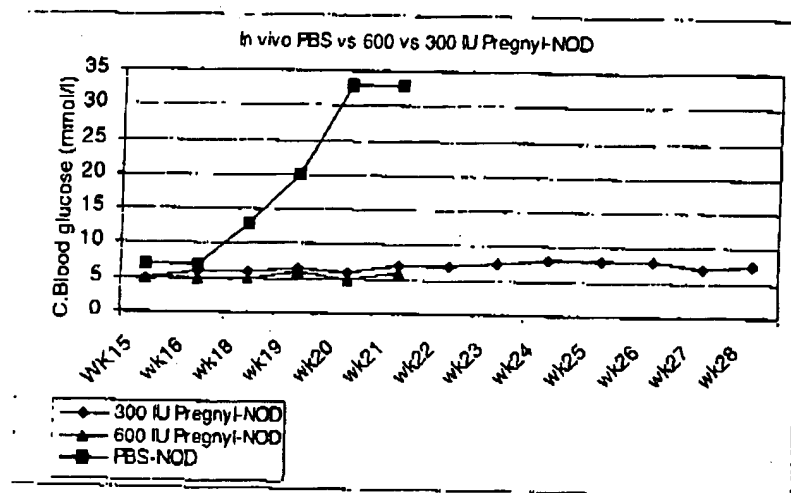


Figure 3.

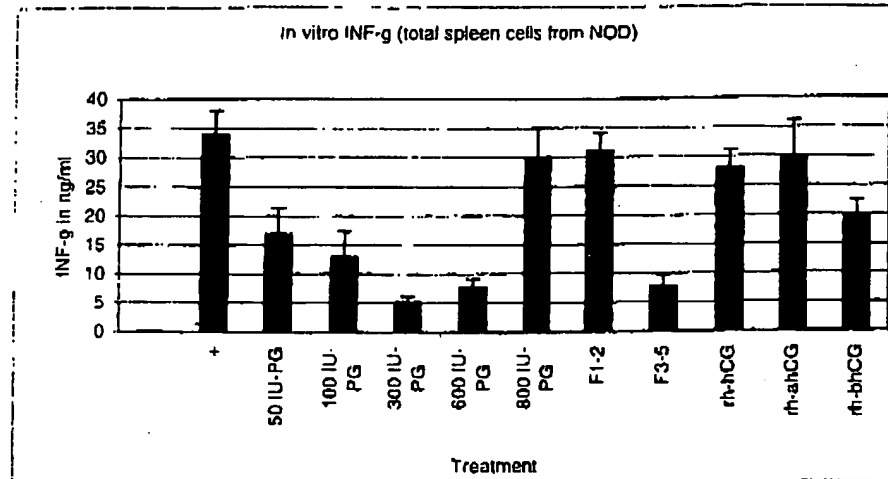


Figure 4.

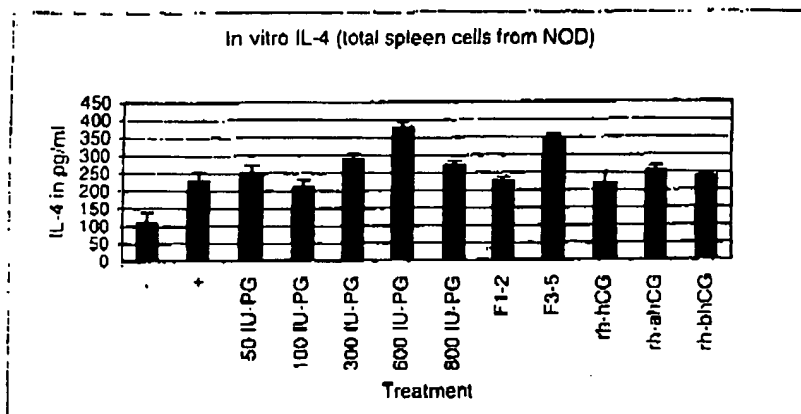


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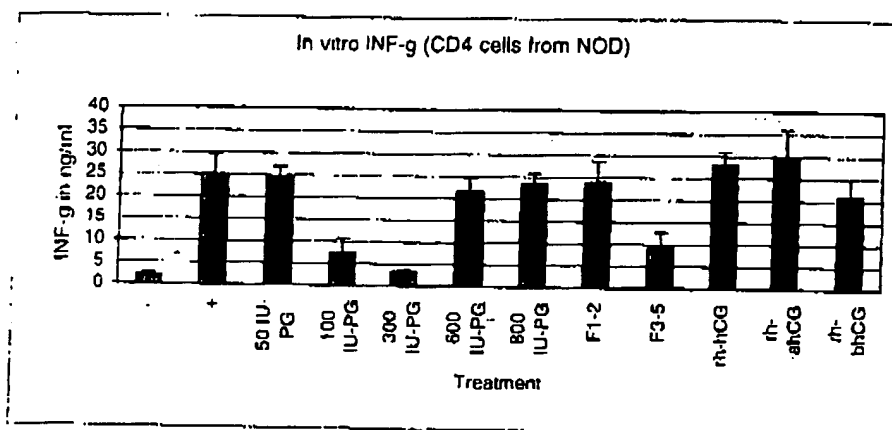
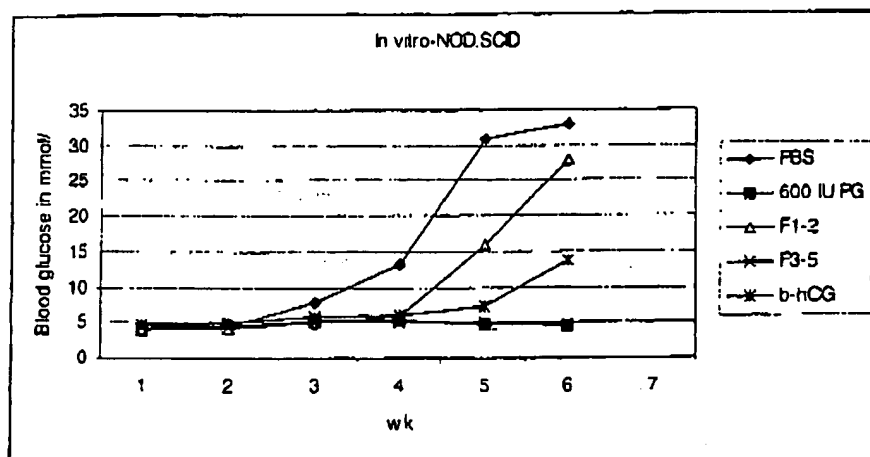


Figure 6.

*Figure 7*

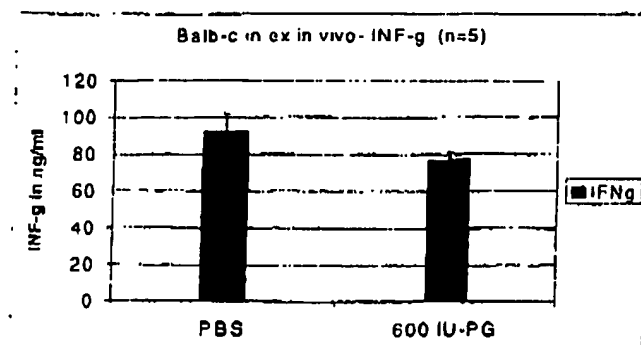


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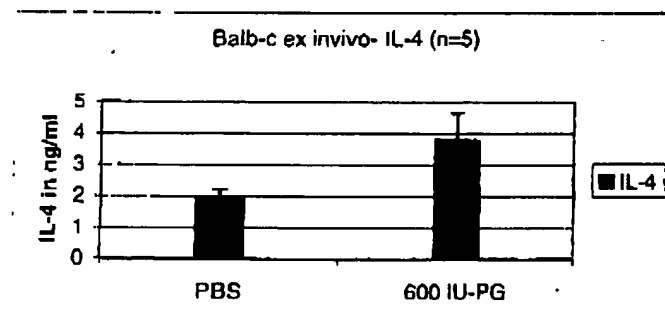


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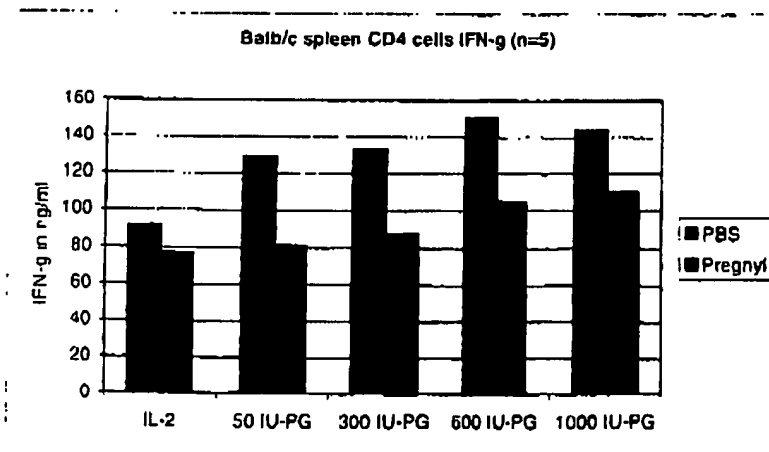
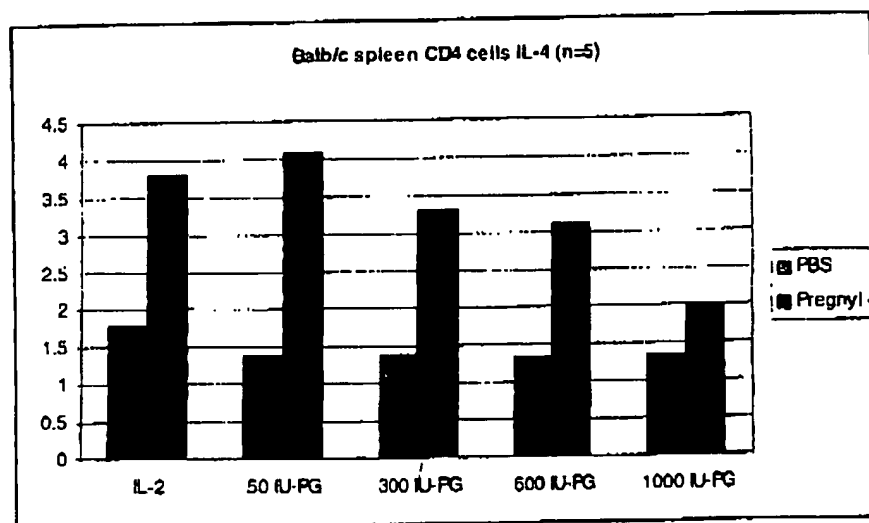


Figure 10.

*Figure 11.*

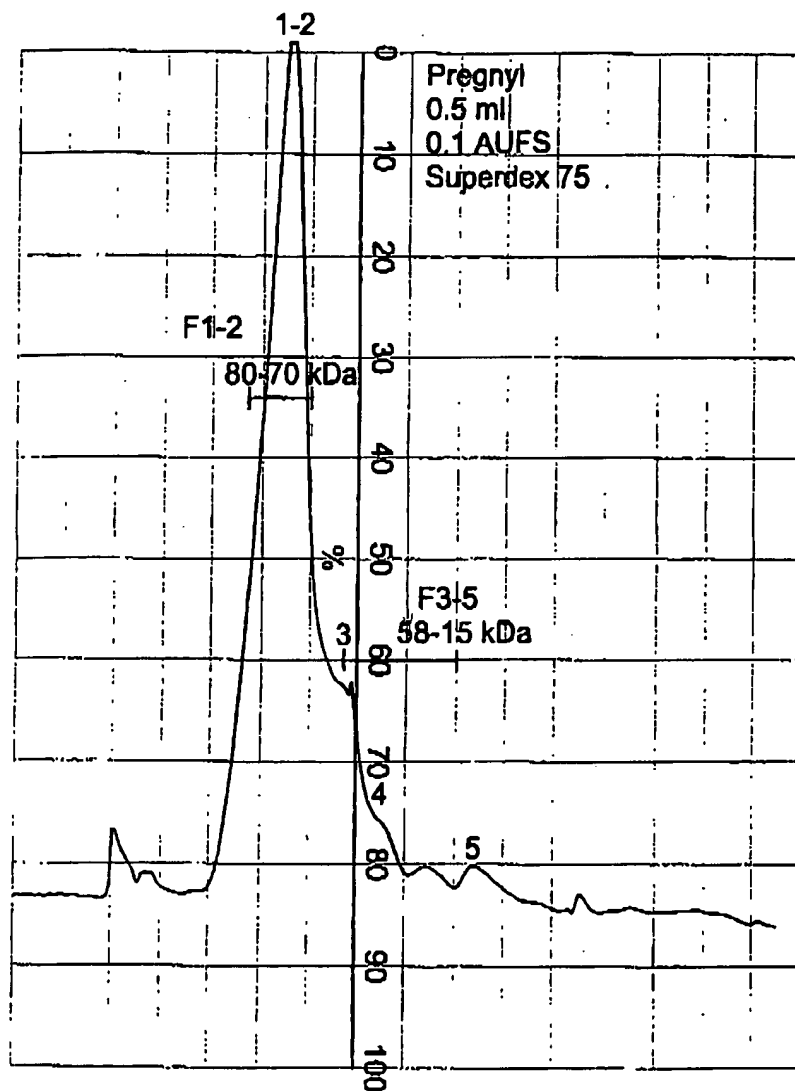


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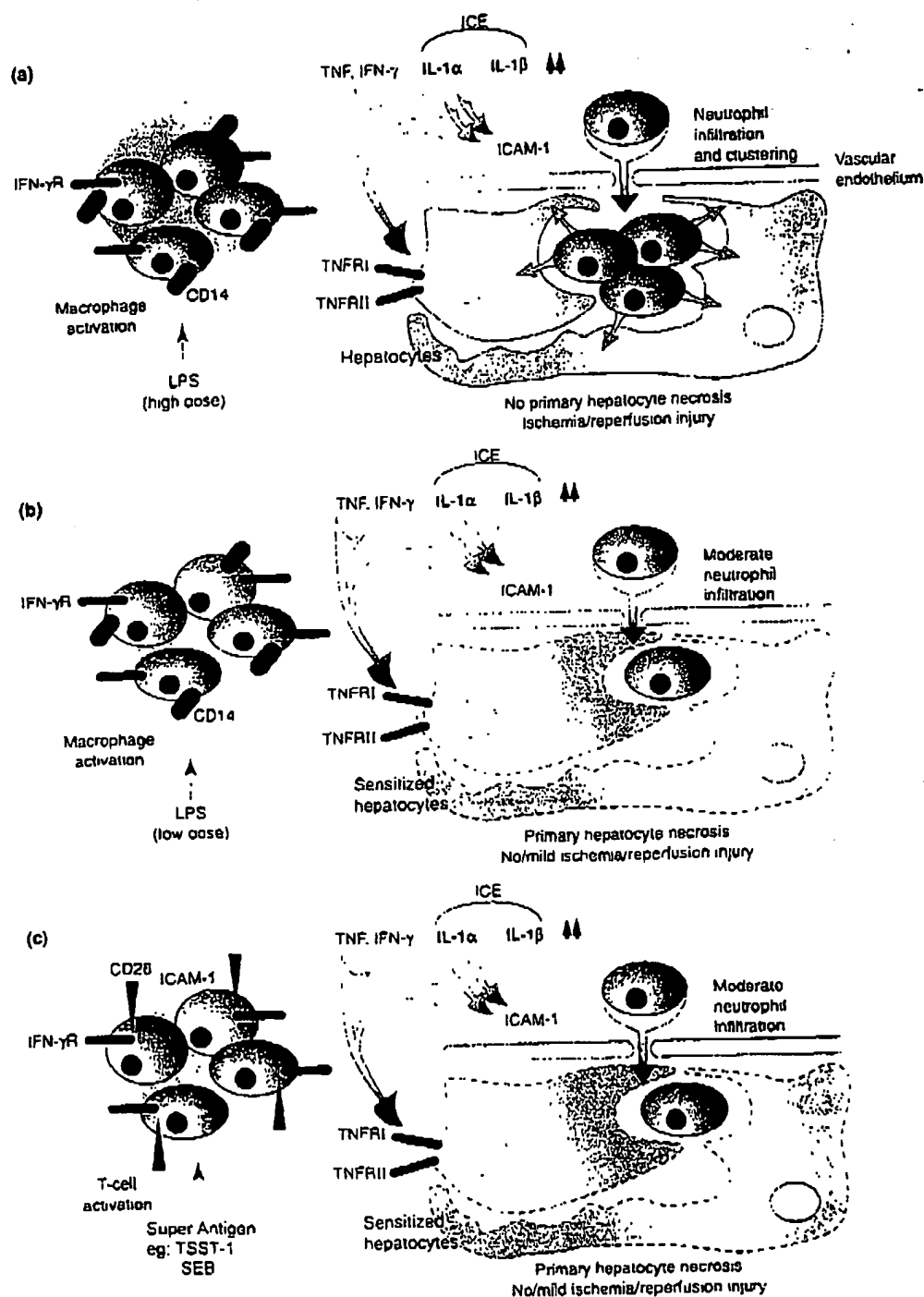


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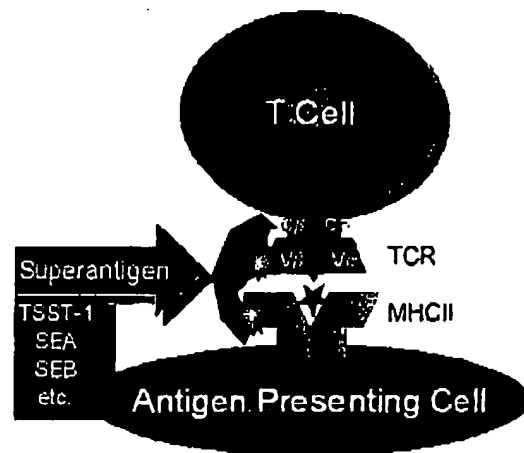


Figure 14

[illegible]

Figure 15

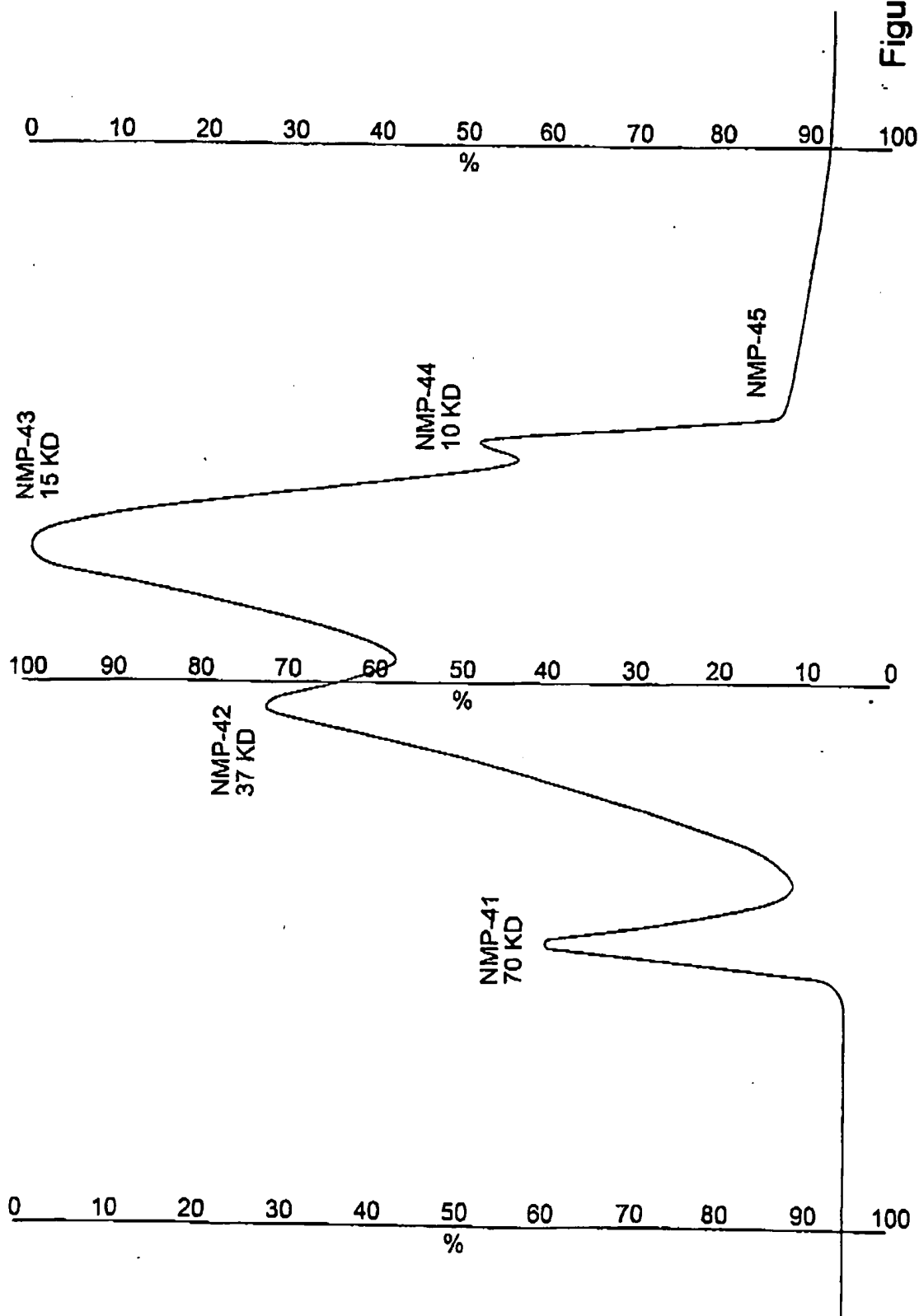
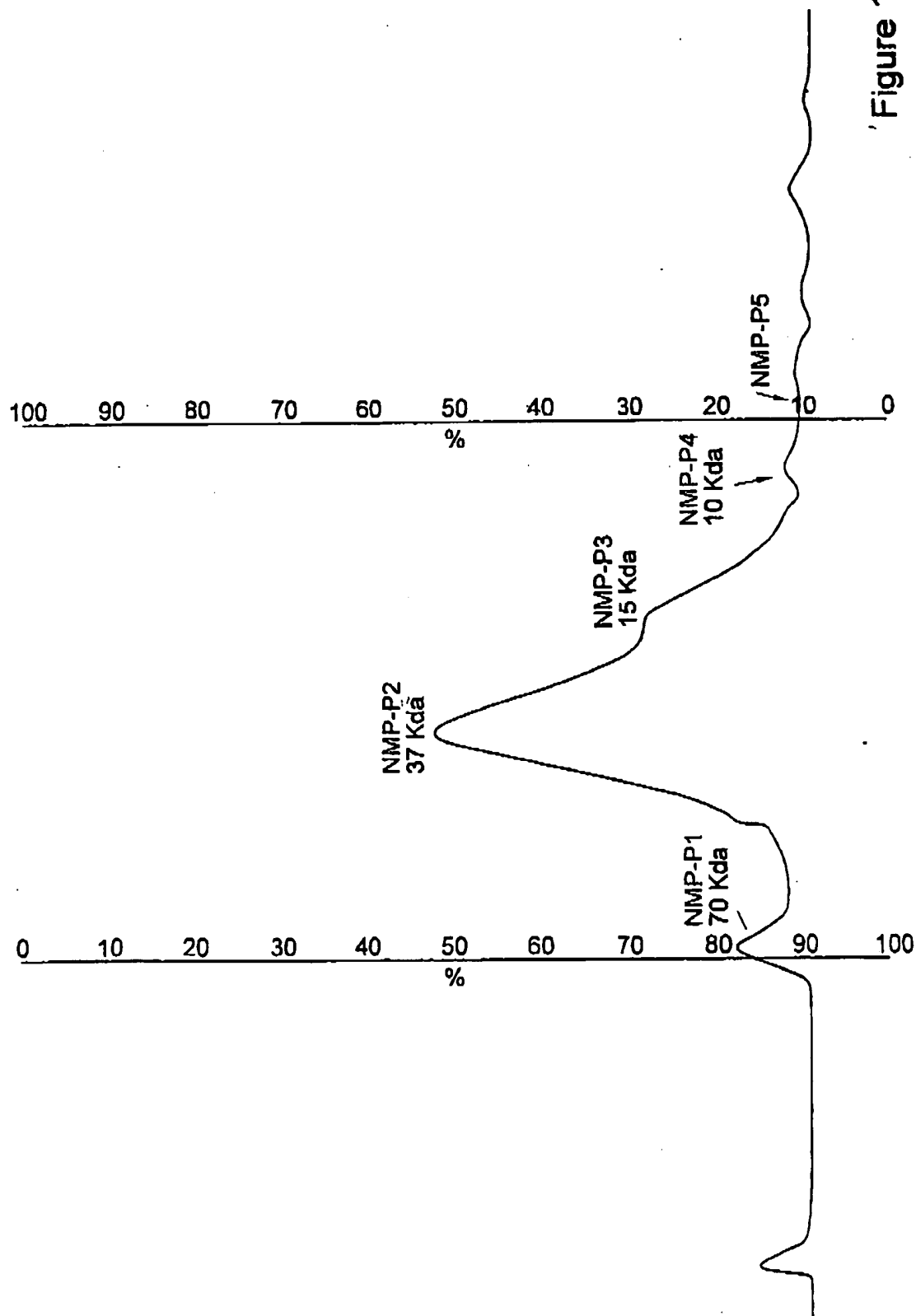


Figure 16



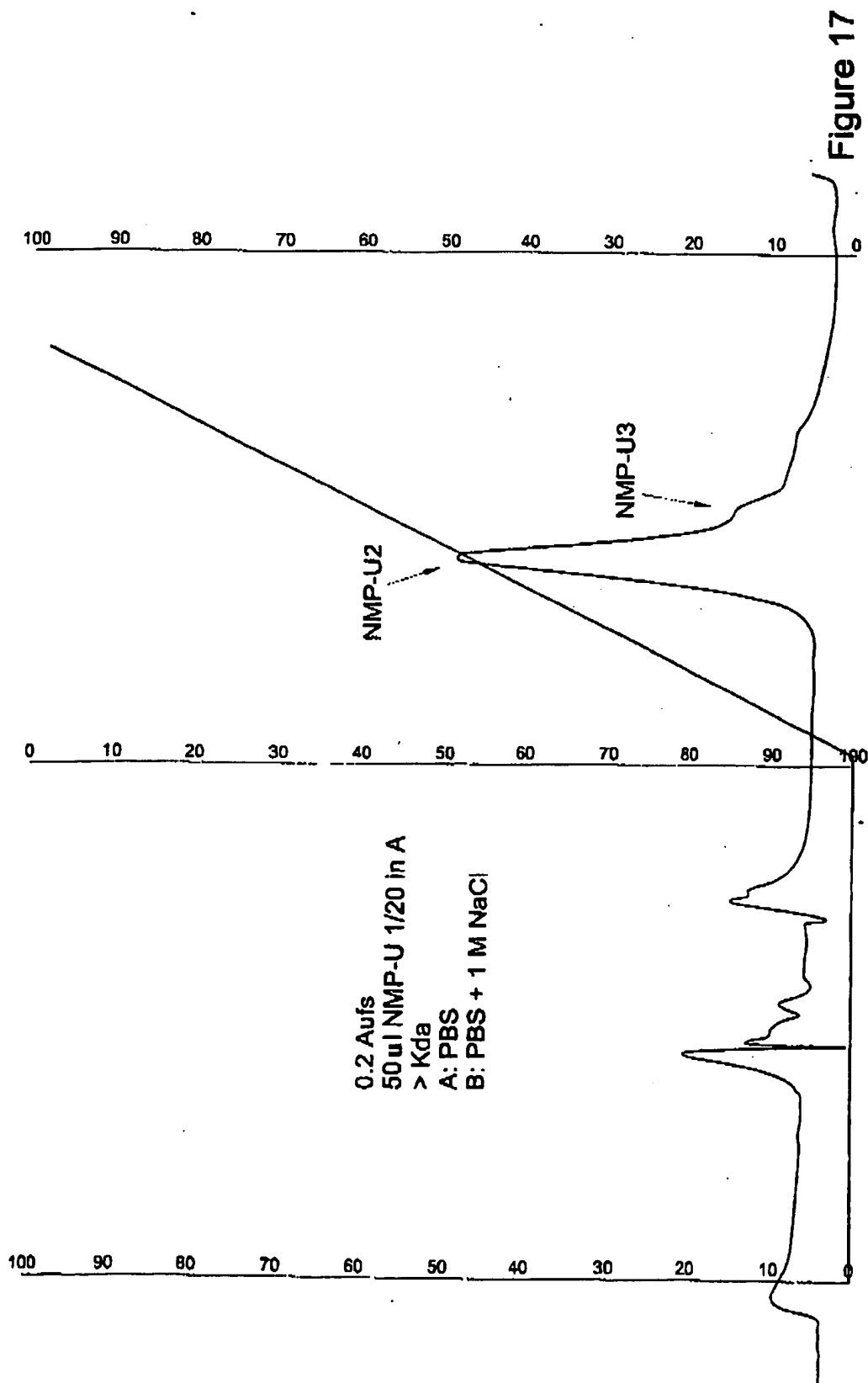


Figure 18

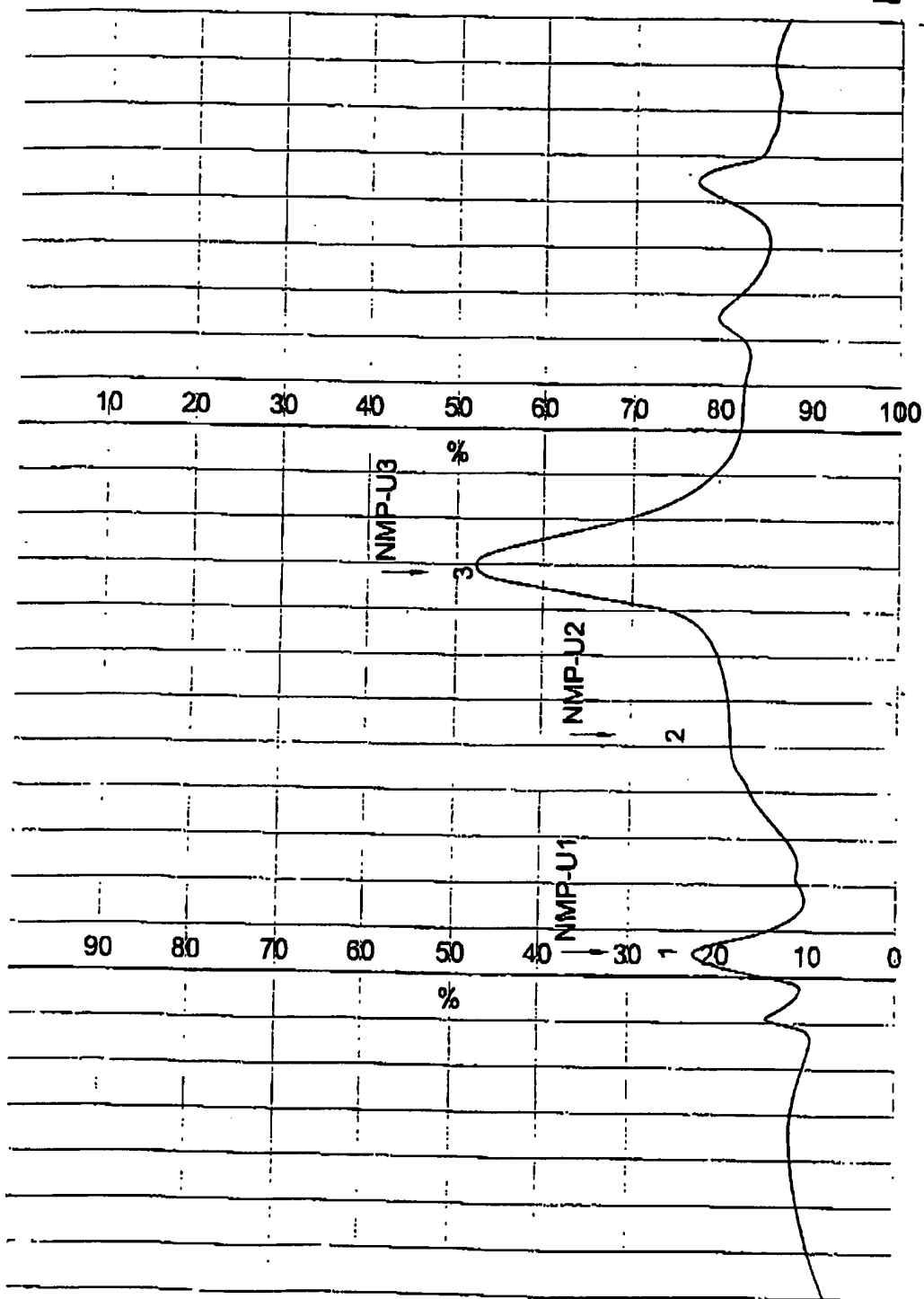
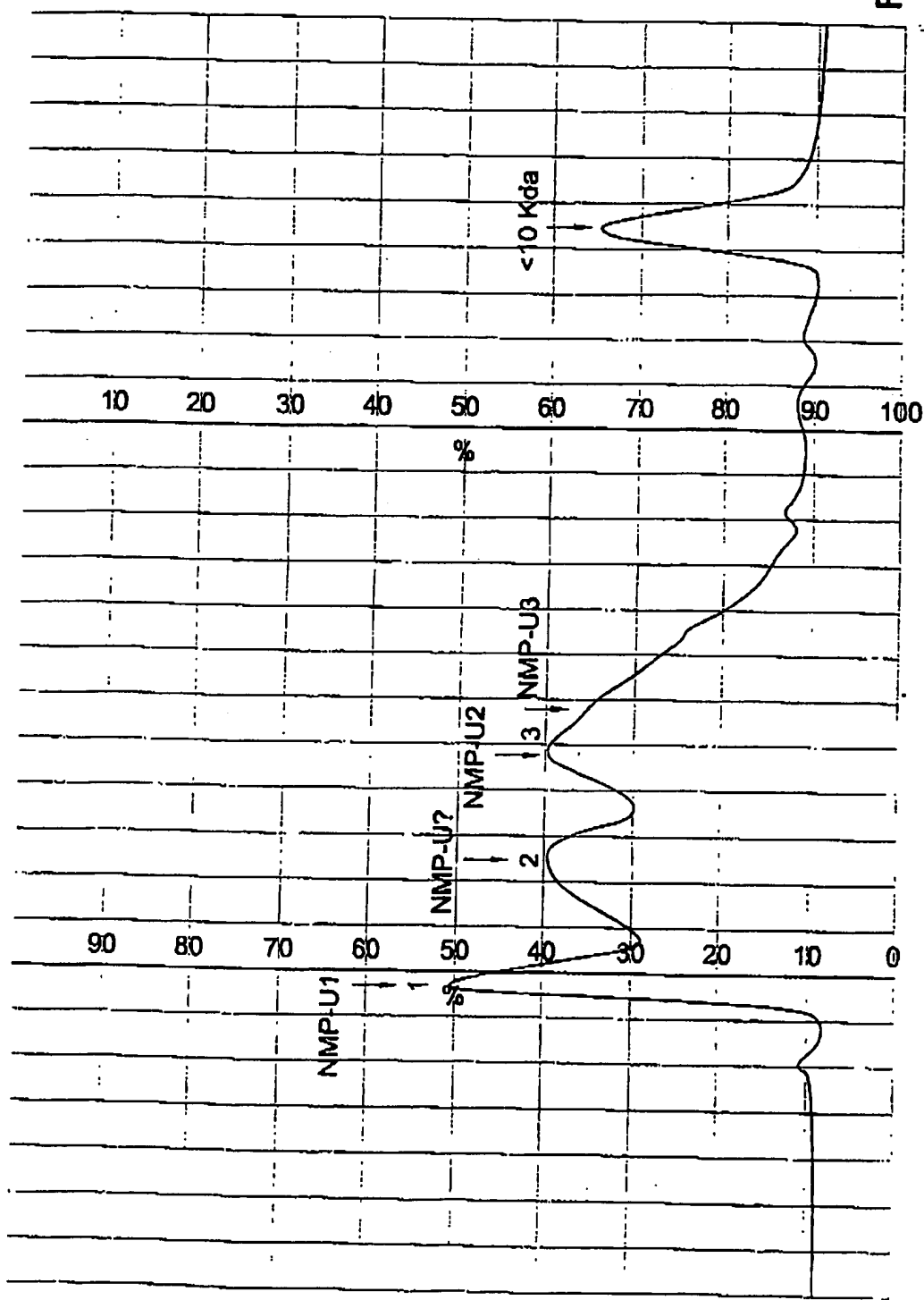


Figure 19



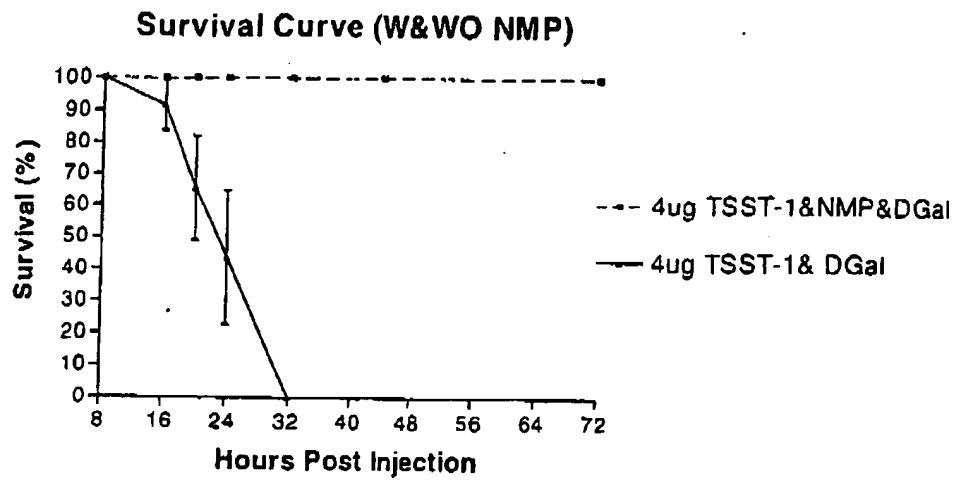


Figure 20

Comparison of Illness Kinetics during Toxic
Shock Between NMP and non-NMP treated mice

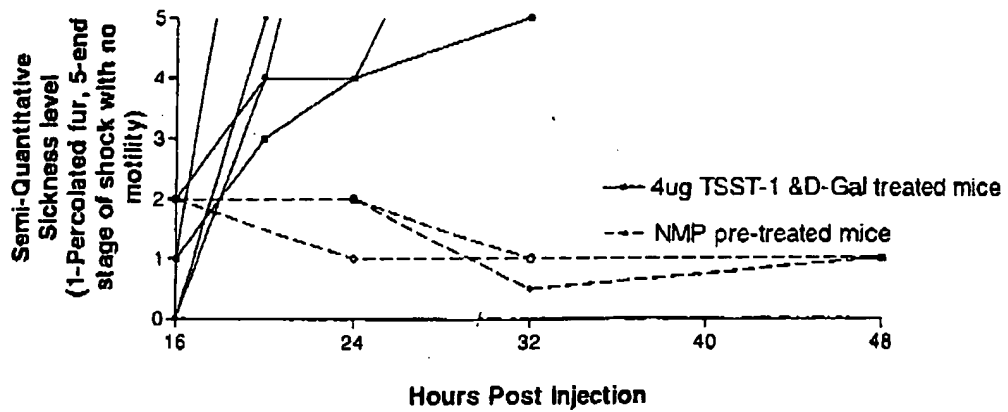


Figure 21

Comparison of Weight Loss
during Toxic Shock with and
without NMP Pretreatment

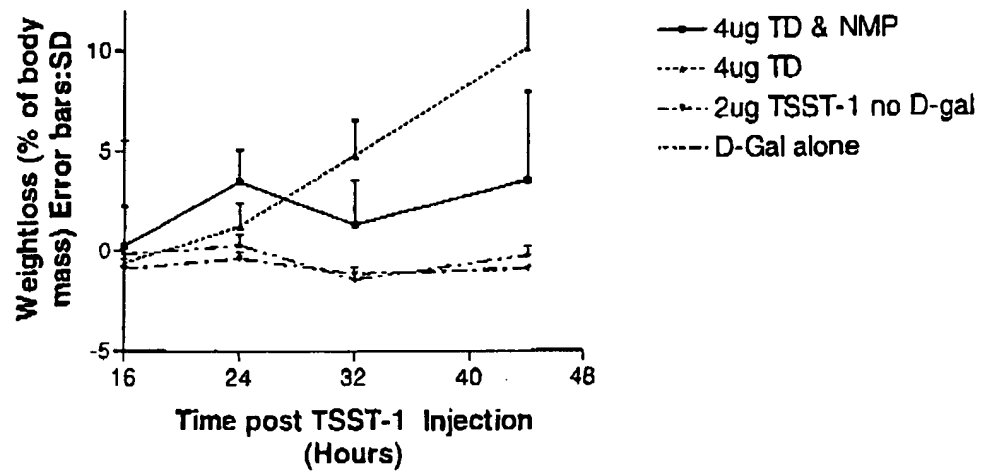


Figure 22

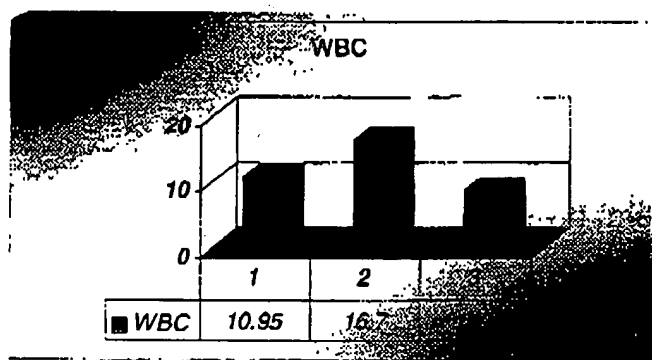


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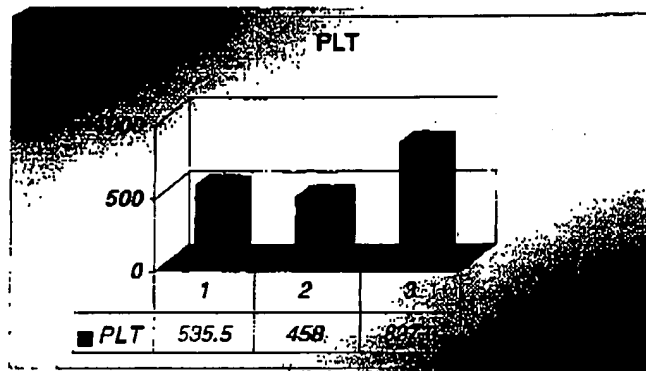


Figure 24

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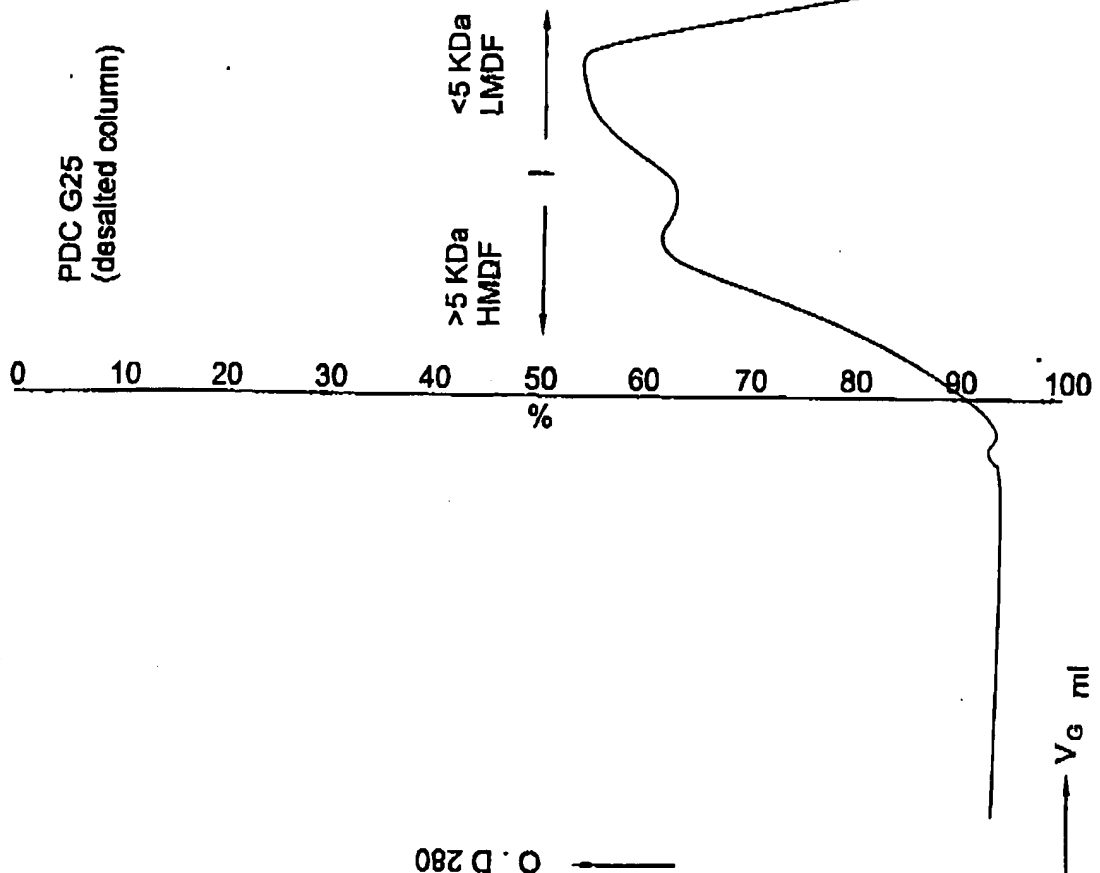
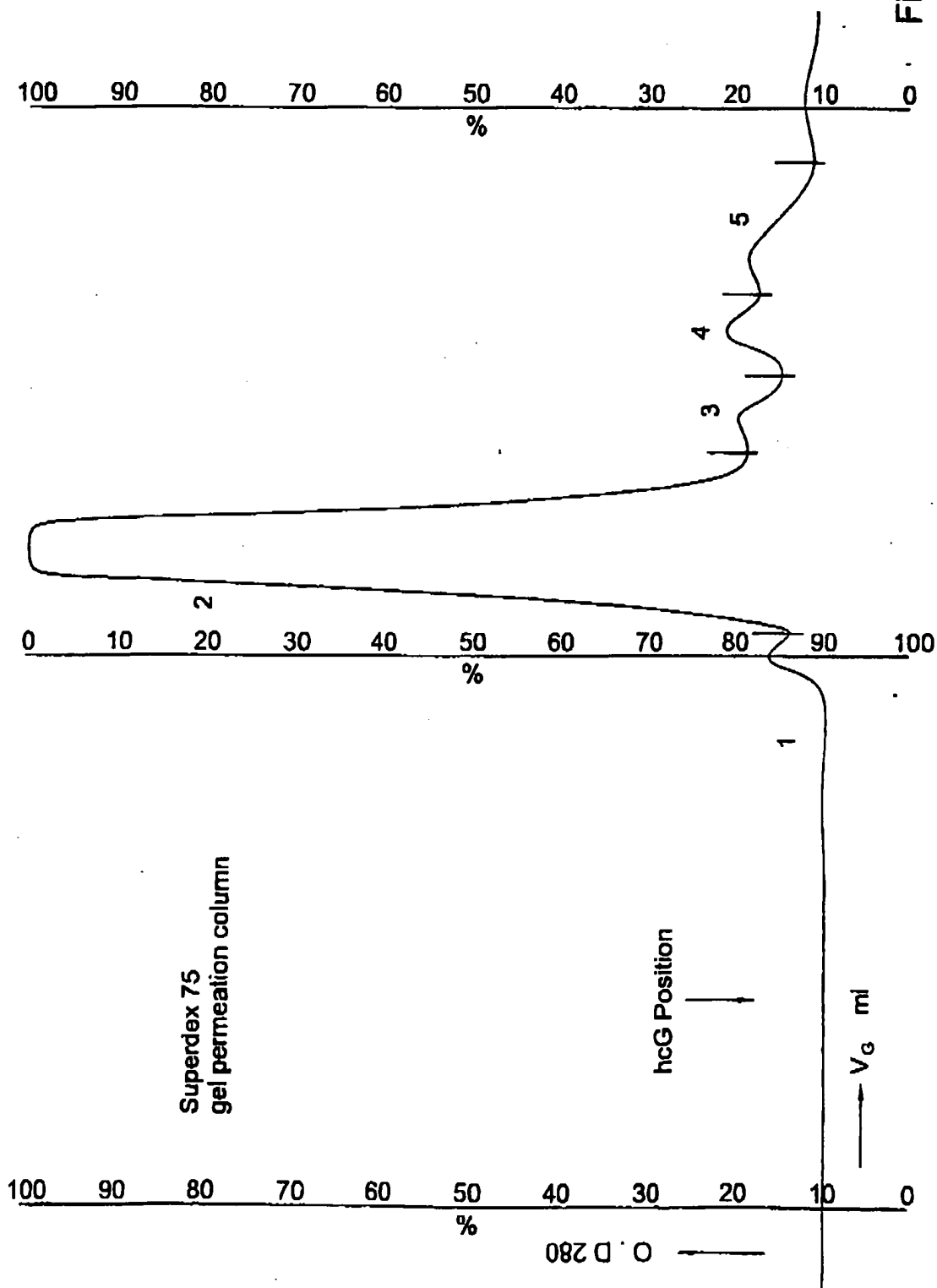


Figure 25

Figure 26



superdex peptide, PC3,2/30

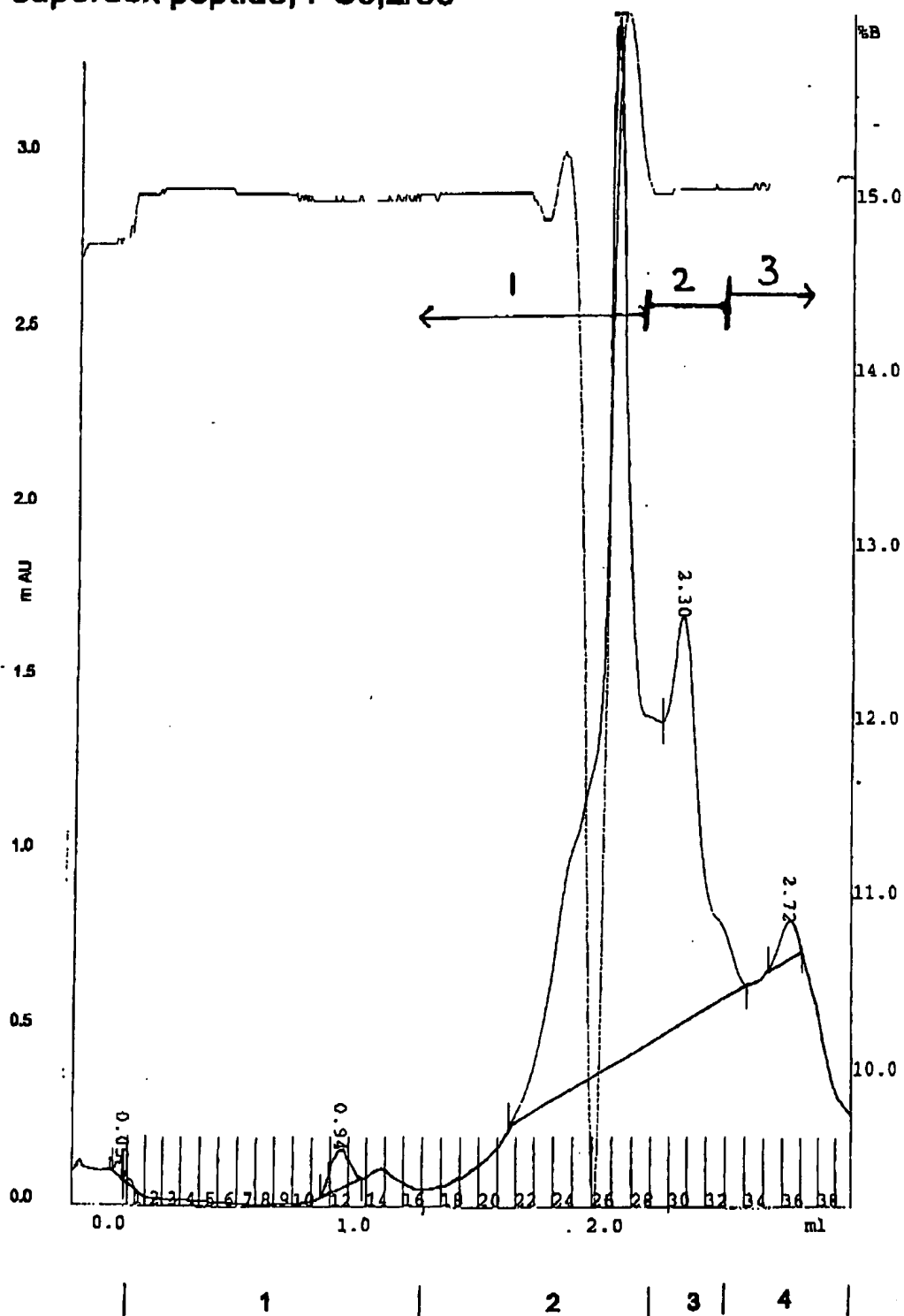


Figure 27

SUBSTITUTE SHEET (RULE 26)

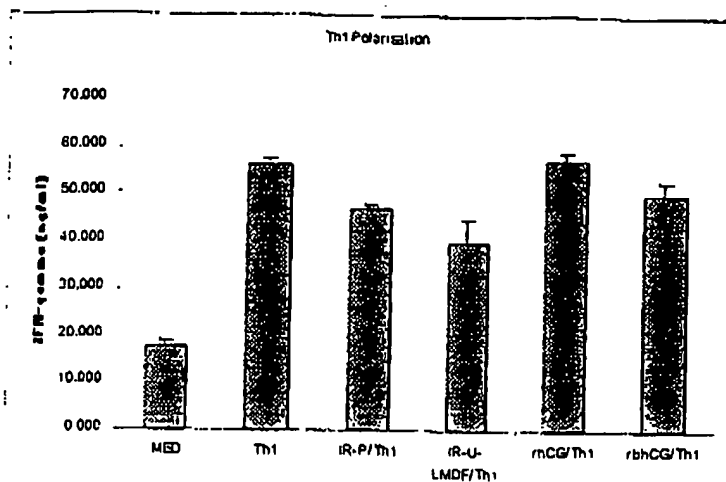


Figure 28. This figure shows that there is strong inhibition of IFN-gamma production found with IR-P and IR-U/LMDF on CD4⁺ cells polarizing towards Th1 phenotype (in vivo). There was only a moderate inhibition of IFN-gamma production observed with recombinant beta-hCG and no effect was seen with recombinant hCG as compare to control (MED).

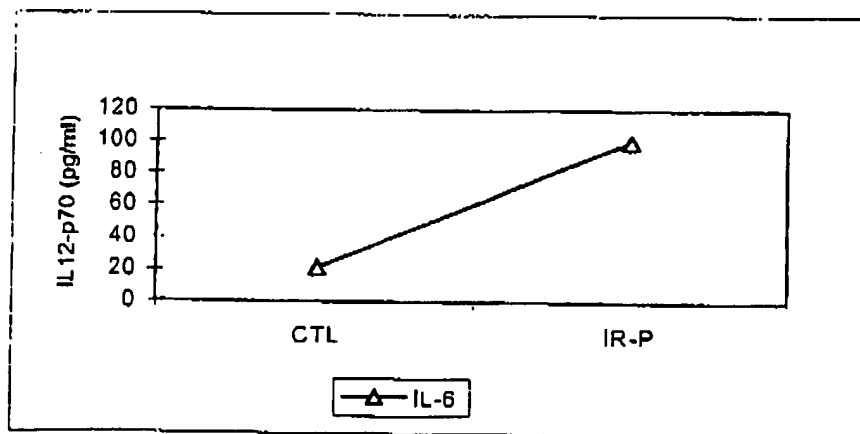


figure 45

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Figure 29

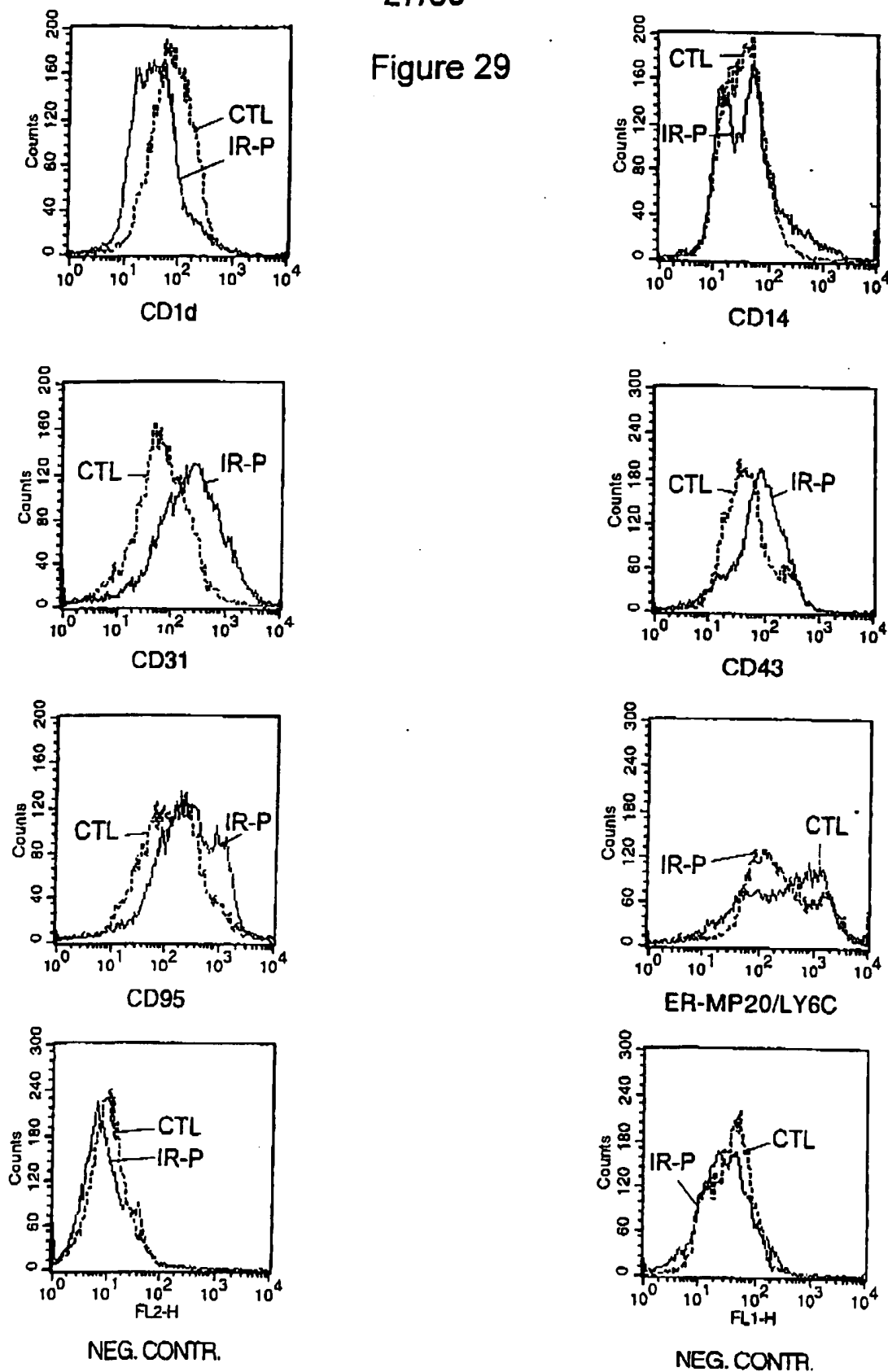
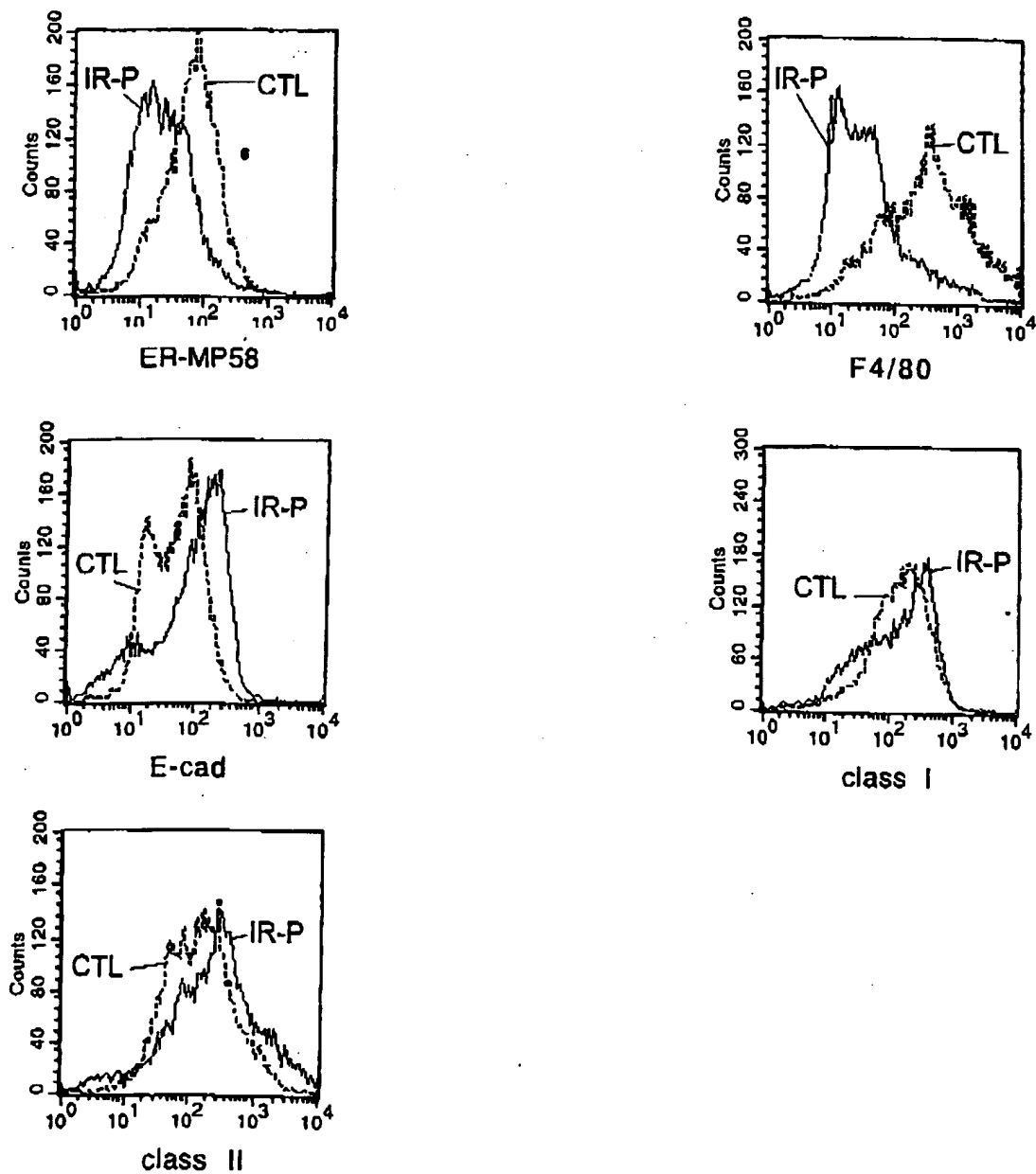


Figure 29



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Figure 30

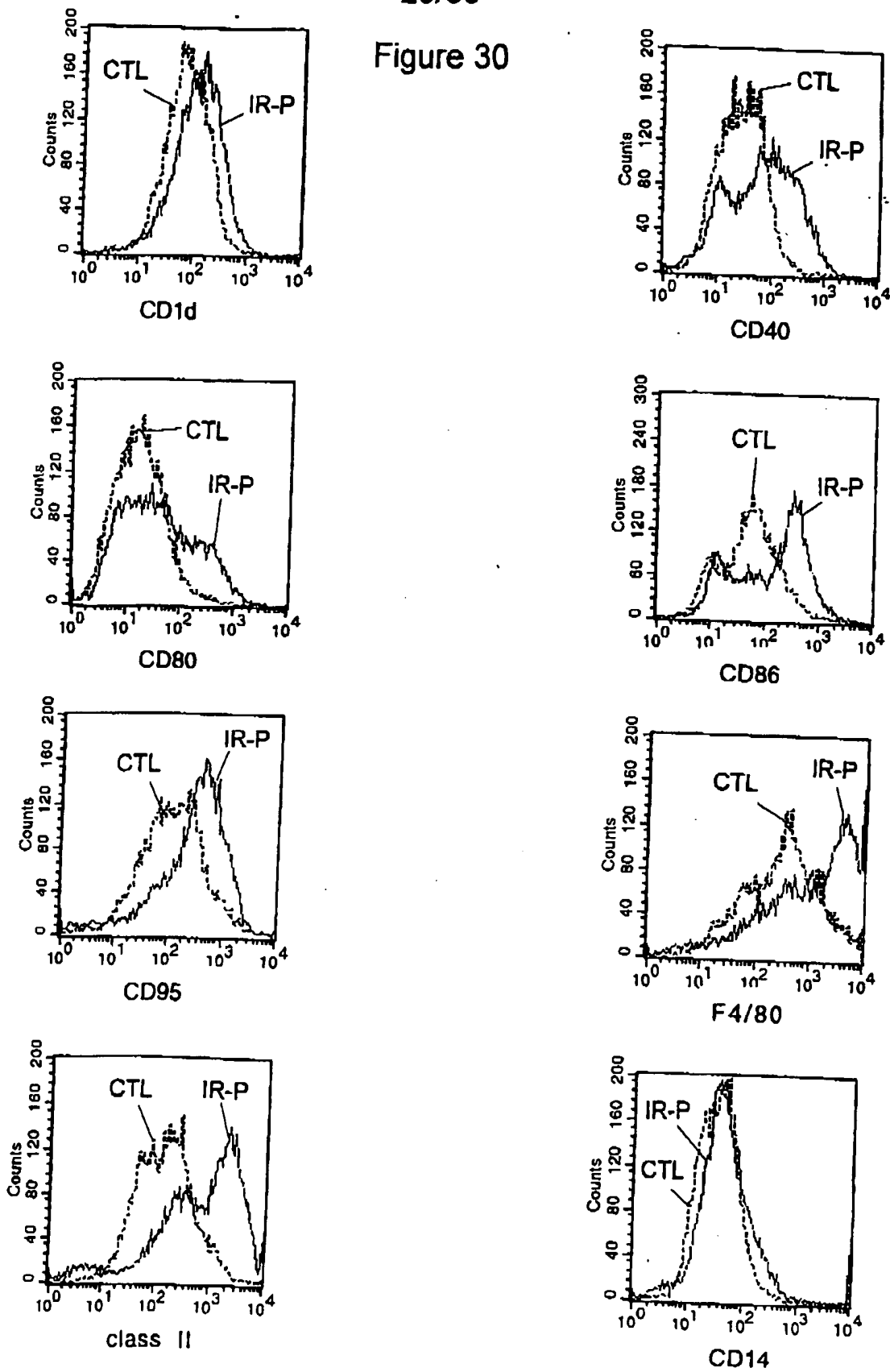
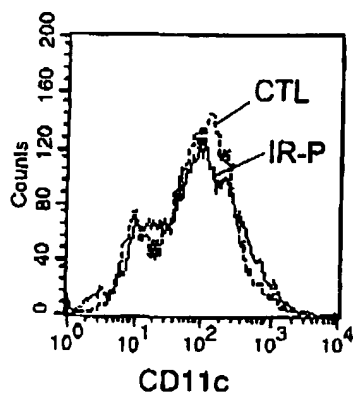
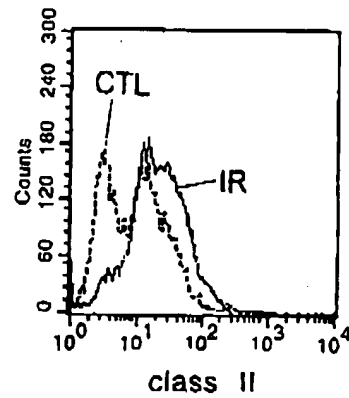
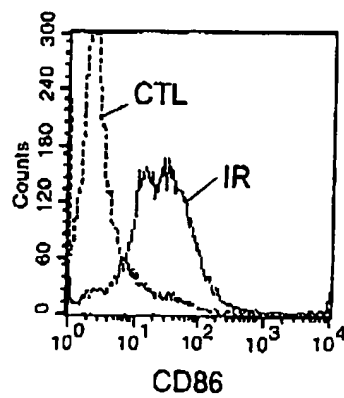
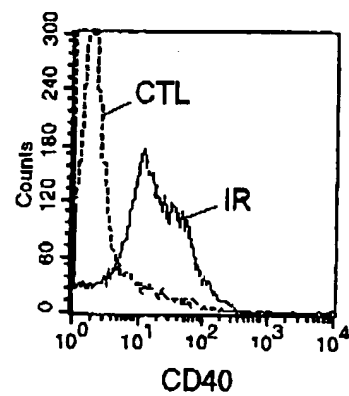
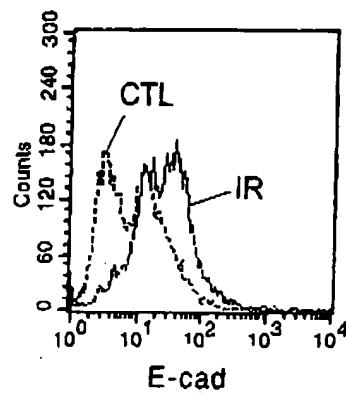
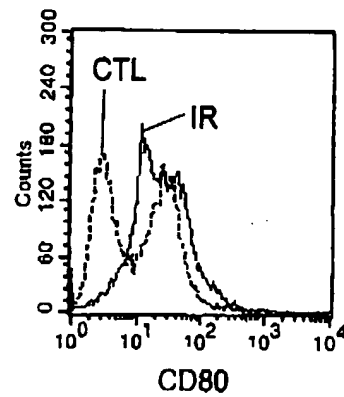
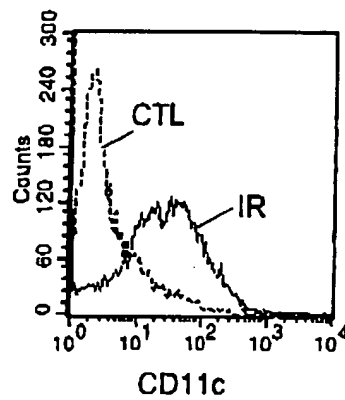


Figure 30



SECRET

Figure 31



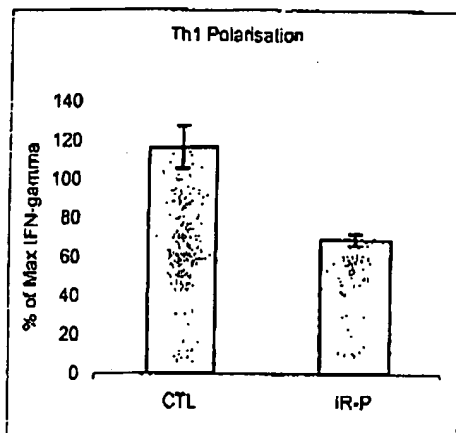


Figure 32 shows that due to the IR-P treatment in Balb/c mice the CD4⁺ cell are shifted towards Th2 phenotype, showed by the inhibition of IFN-gamma production as compare to control (CTL) group.

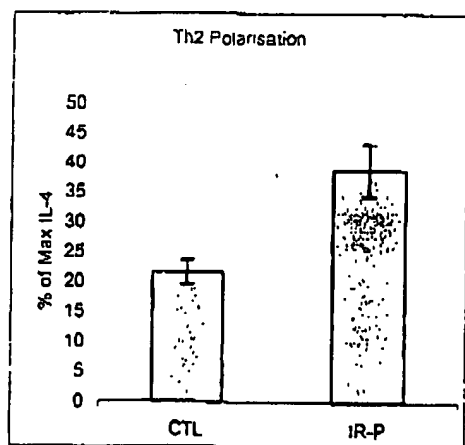


Figure 34 shows that due to the IR-P treatment in Balb/c mice the CD4⁺ cell are shifted towards Th2 phenotype, showed by the increase in IL-4 production as compare to control (CTL) mice.

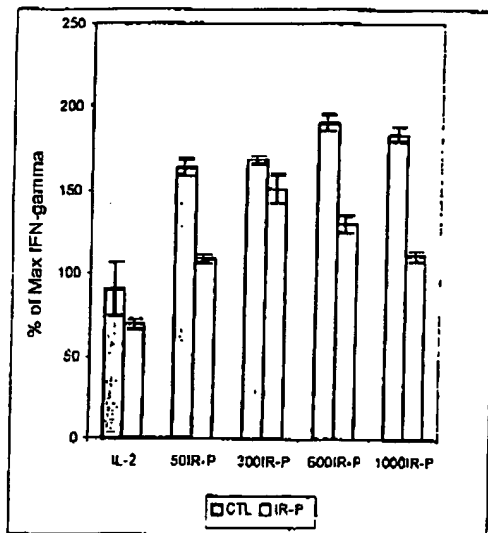


Figure 36 shows that CD4+ T cells from PBS and IR-P mice treated (in vivo) with different doses of IR-P (in vitro) show increase in IFN-gamma production which suggest the shift towards Th1 phenotype (see also figure 37).

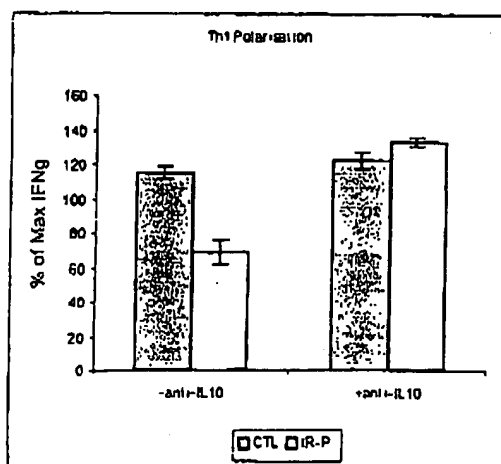


Figure 38 shows an increase in IFN-gamma production in Th1 polarization conditions in IR-P group, which suggests that the promoting effect of IR-P on Th2 subset is at least IL-10 dependent (for detail see text).

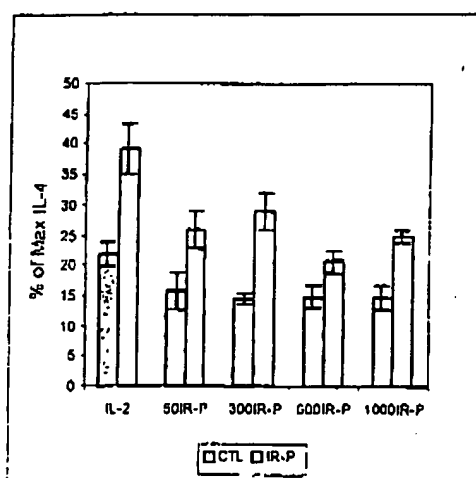


figure 37 shows that CD4+ T cells from PBS and IR-P mice treated (in vivo) with different doses of IR-P (in vitro) show decrease in IL-4 production which suggest the shift towards Th1 phenotype (see also figure 36).

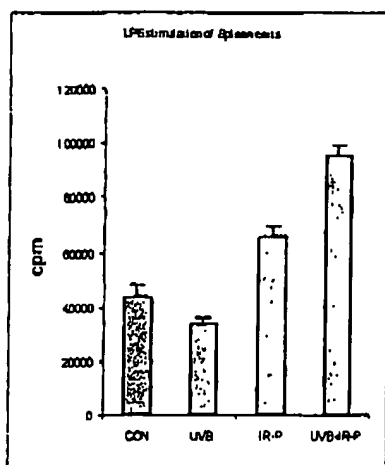


Figure 46.

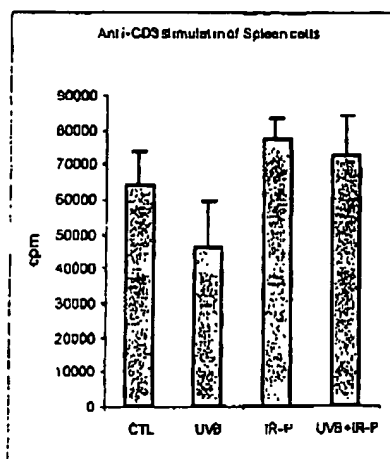


Figure 47.

LPS and anti-CD3 stimulated proliferation of spleen cells from UVB and IR treated Balb/c mice. Reduction in LPS and anti-CD3 proliferation was observed in UVB treated Balb/c mice (figure 46, 47)) while IR or combined IR and UVB-irradiated treated mice had increase LPS and anti-CD3 stimulated proliferation (figure 46, 47).

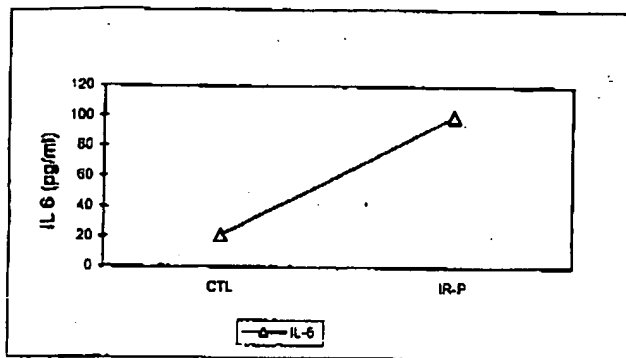


figure 45 shows that LPS stimulated spleens cells from IR treated Balb/c mice produce high level of IL-6 (ex vivo) as compare to control (CTL) group treated with PBS

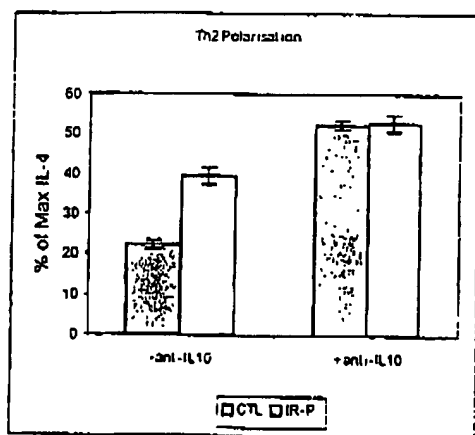


Figure 39 shows increase in IL-4 production in Th2 polarization conditions seen with anti-IL10 invitro treatment in control (CTL) group and in IR-P group. This suggests involvement of IL-10 in Th1/Th2 polarisation (for detail see text).

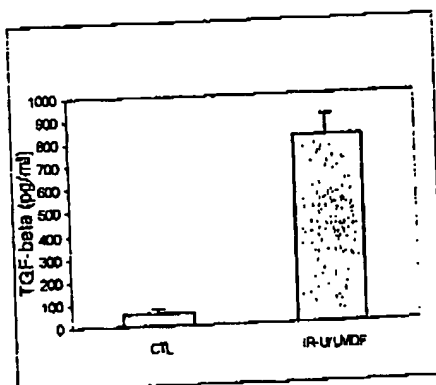


Figure 43

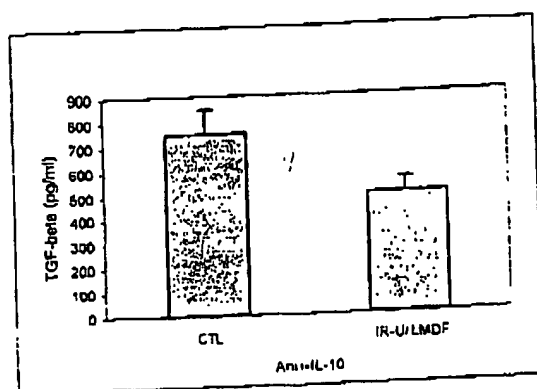


Figure 44 A.

FOR DETAIL SEE DOCUMENT

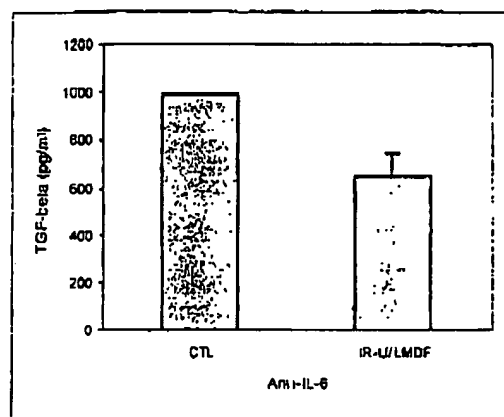


Figure 44 B

FOR DETAIL SEE DOCUMENT

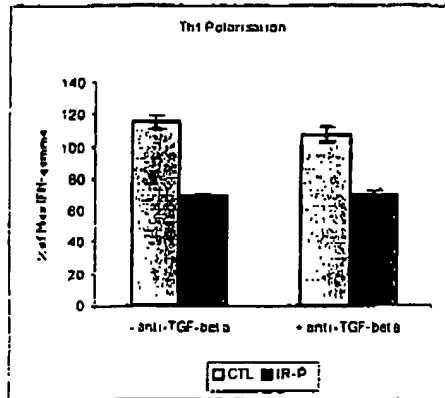


Figure 40.

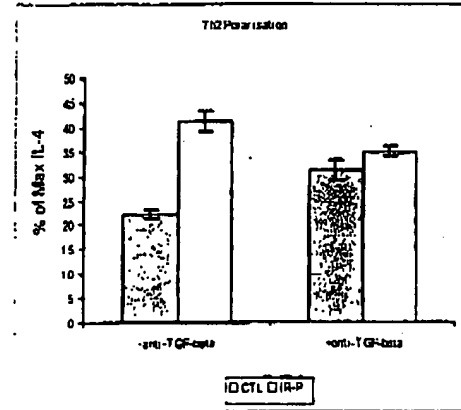


Figure 41

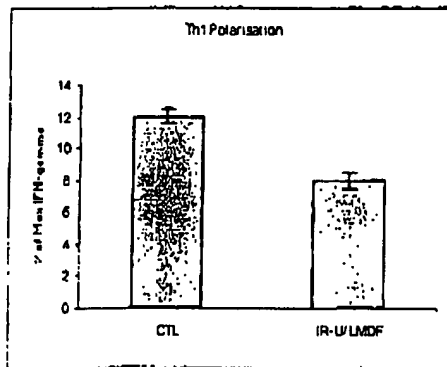


Figure 33.

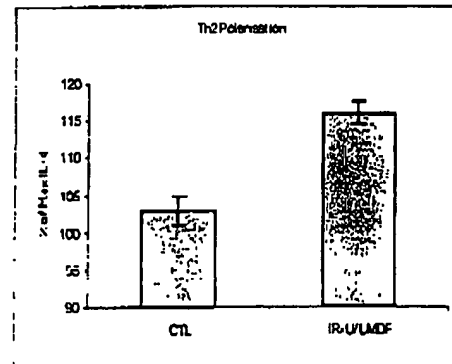


Figure 35.

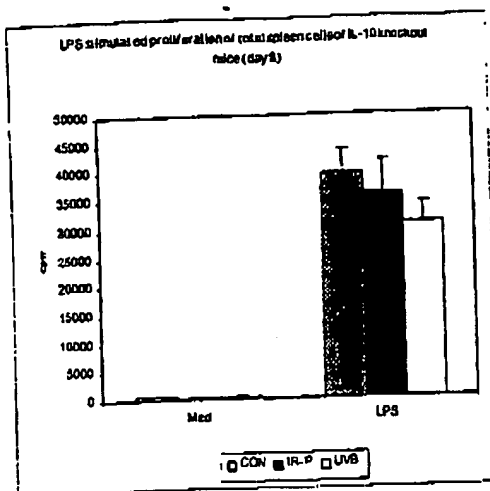


Figure 50

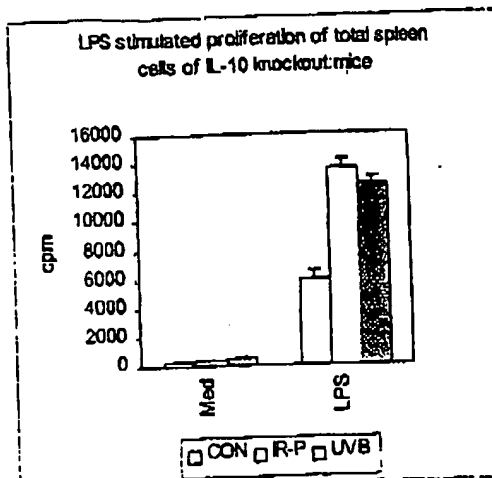


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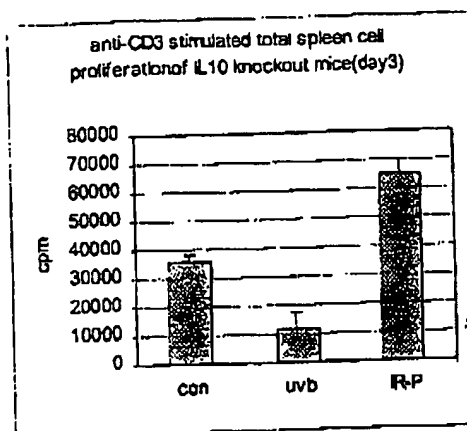


Figure 48

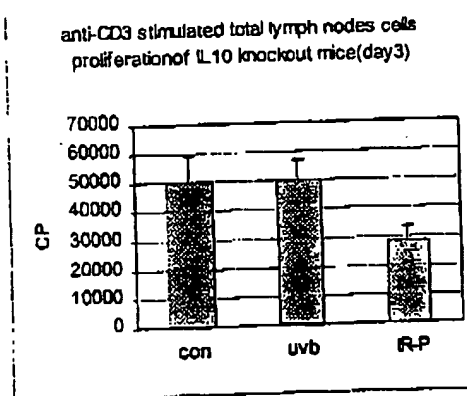


Figure 49

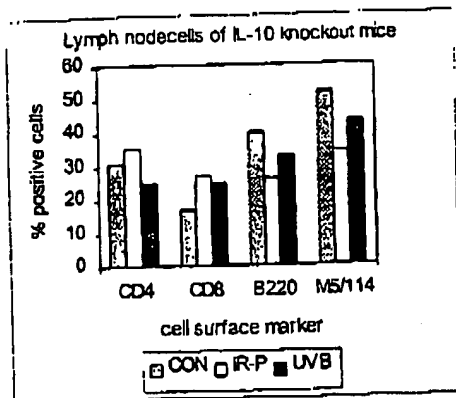


Figure 52

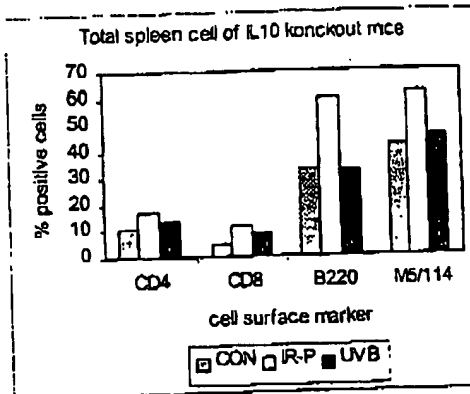


Figure 53

Mab	Med	IR-P	IR-U	IR-U3-5	IR-U/LMDF
CD1d	4.9	3.2	2.4	2.8	2.8
CD14	0.0	0.6	2.7	1.0	0.8
CD40	0.0	0.0	0.0	0.0	0.0
CD80	0.3	0.0	0.0	0.0	0.0
CD86	1.9	0.8	0.1	0.5	0.6
(all)					
CD95 (all)	5.3	4.1	12.8	5.6	5.6
CD95L	0.2	0.3	0.2	0.0	0.0
ER-MP58	3.9	2.6	1.7	0.0	1.1
F4/80 (all)	39.5	20.1	1.3	2.2	0.0
RB6.8C5		3.6	5.8	5.0	4.1
E-cad	1.9	4.5	0.5	0.5	0.9
(all)					
MHC II	13.6	7.8	9.3	6.3	0.0

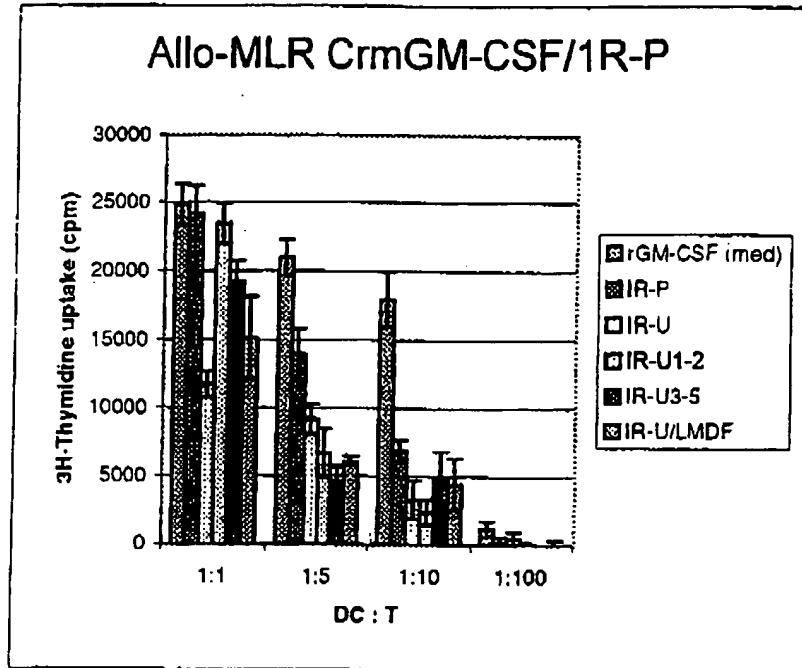
Figure 54

Mab	Med	IR-P	IR-U	IR-U3-5	IR-U/LMDF
CD1d	4.9	7.0	11.8	9.5	9.5
CD14	0.0	1.0	0.9	1.9	1.2
CD40	0.0	0.6	4.4	5.5	3.8
CD80	0.3	0.3	0.9	0.7	0.6
CD80 (fractic)			8.0 (37%)	16.0 (20%)	12.8 (20%)
CD86	1.9	3.3	19.7	10	11.5
(all)					
CD95	5.3		15.2	16	16
ER-MP58	3.9	5.2	6.1	7.7	7.0
F4/80 (all)	39.5	32.2	108.8	136.9	155.
RB6.8C5		7.7	8.2	4.0	4.3
E-cad	1.9	2.1	3.2	3.3	1.9
(all)					
MHC II (all)	13.6	18.1	108.8	94.5	109.6

Figure 55

FOR MORE DETAILS. SEE DOCUMENT

Figure 56



FOR MORE DETAILS, SEE DOCUMENT

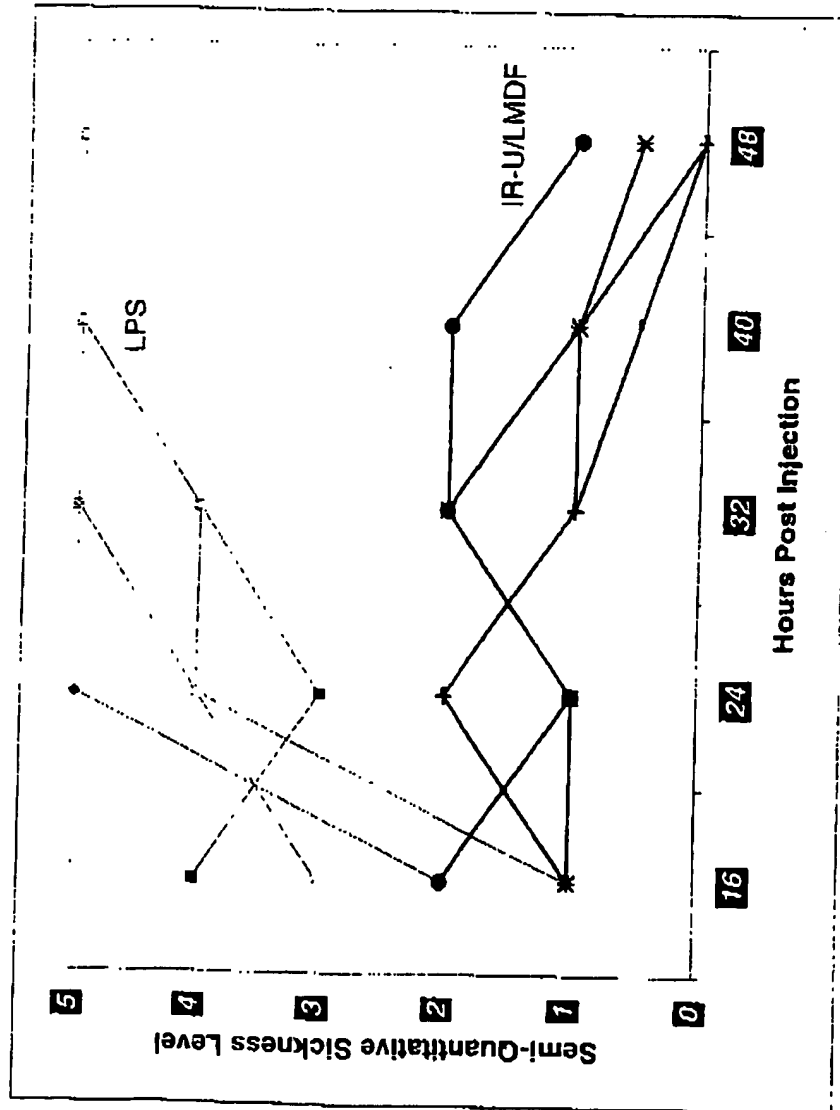


Figure 57

FOR DETAIL, SEE DOCUMENT

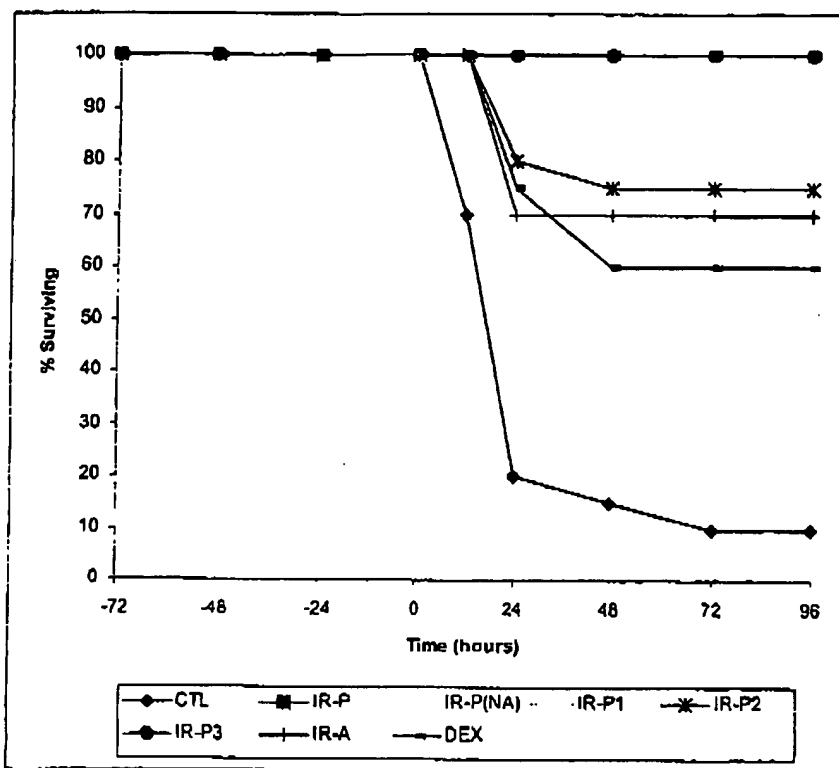


Figure 58. To determine the effect of high-dose LPS treatment in IR treated mice, Balb/c mice (n=30) were injected intraperitoneally with LPS (150 mg/kg) and survival was assessed daily 5 days. PBS-treated Balb/c mice succumbed to shock between days 1 and 2 after high-dose LPS injection, with only 10% of the animals were alive on day 5. In contrast, 100% of IR-P, or its fraction IR-P1, IR-P3 treated mice were alive on day 5 ($P < 0.001$), while IR-P2, IR-A and Dexamethasone treated mice demonstrated around 70% of surviving.

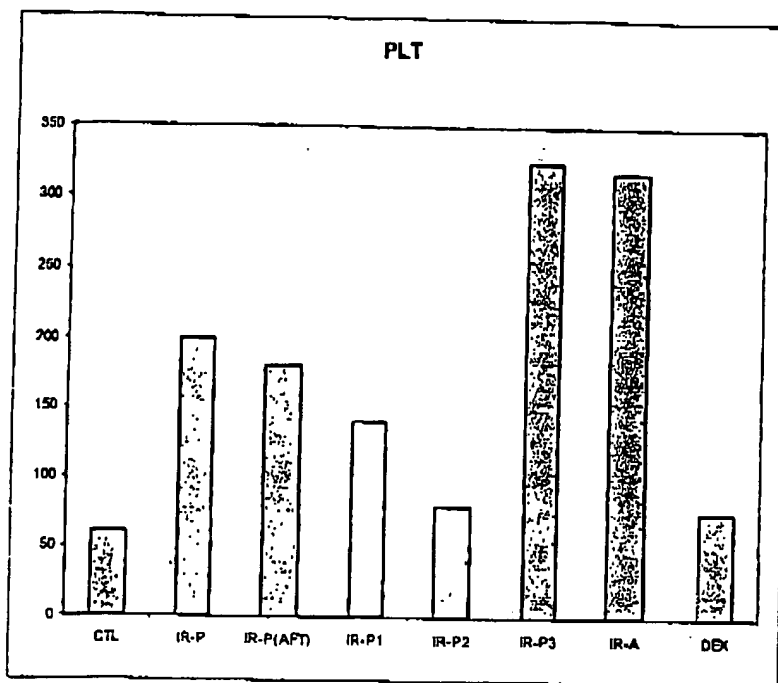


Figure 59 shows that IR-A, IR-P and its fraction IR-P1, IR-P3 have all platelets counts within normal range ($100-300 \times 10^9$), while control, IR-P2 and Dexamethasone treated mice have platelets counts below normal range.

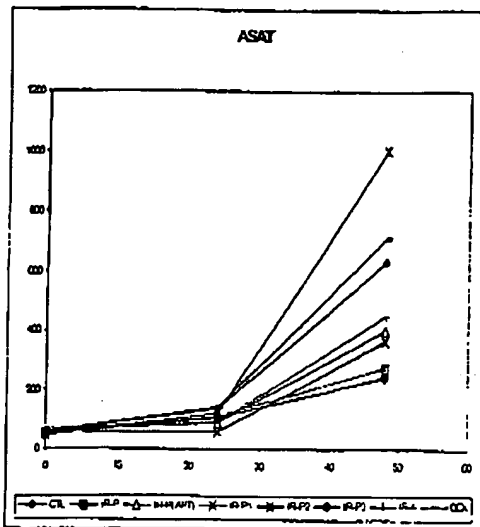


Figure 61

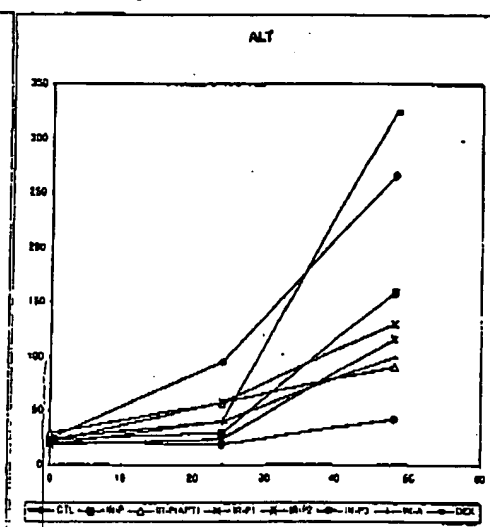


Figure 60

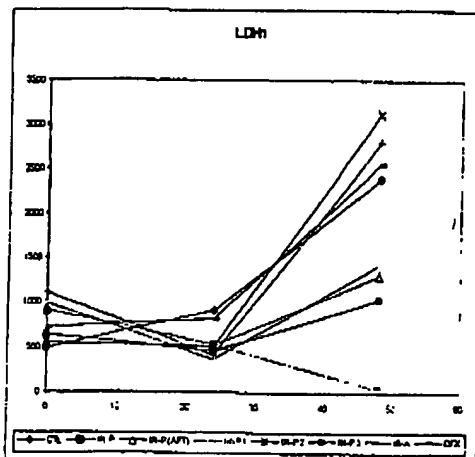


Figure 62

(figure 60-62) shows that mice treated with IR-A, IR-P and its fraction IR-P1, IR-P2, IR-P3 had relatively lower level of ALT, LDH1, ASAT enzymes present in the plasma as compare to control and dexamethasone treated mice. These enzymes are present in higher concentration in blood during shock due to organ damage, so these result are consistant with our surviving results (figure 58).

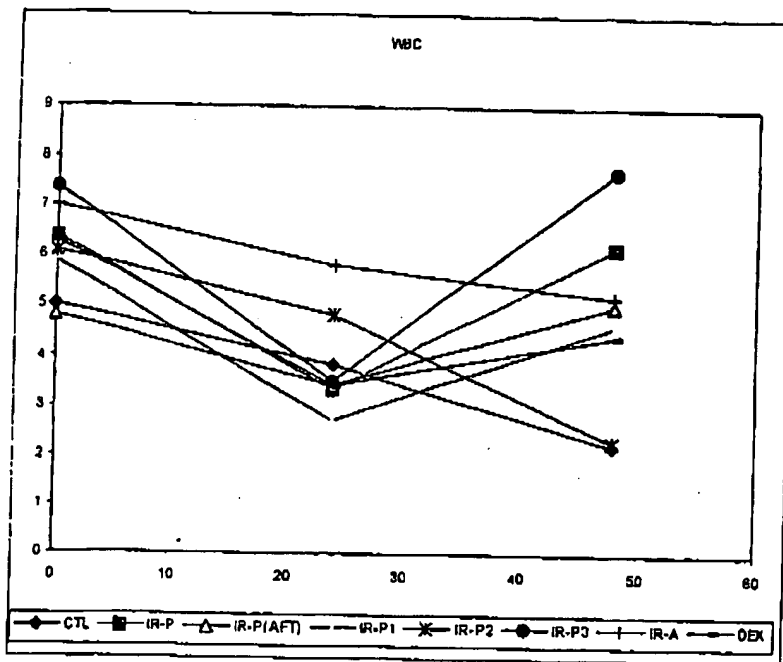


Figure 63 Our results show that mice treated with IR-A, IR-P and its fractions have moderate to normal level of WBC at $t=48$ hours then the control and dexamethasone treated mice, suggesting less inflammatory responses in IR treated mice.

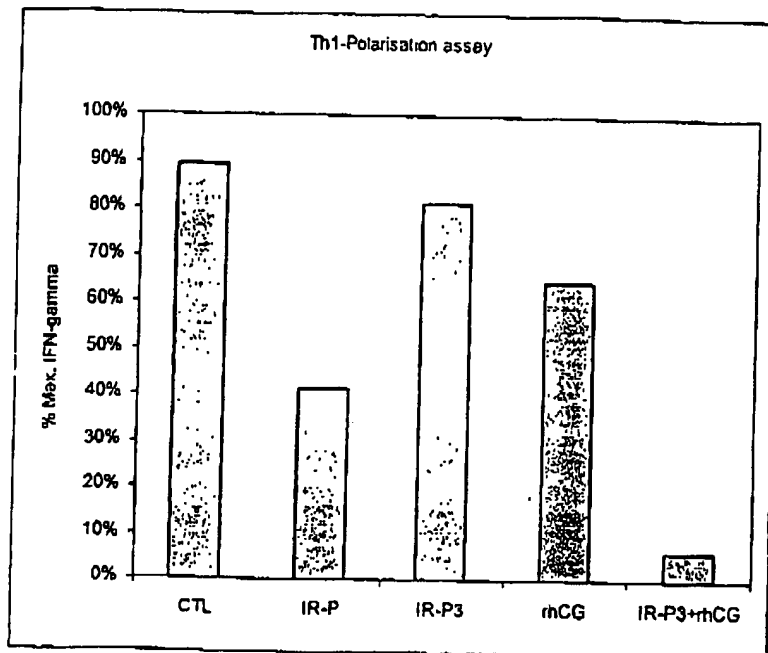


Figure 64 shows inhibition of IFN-gamma production in Th1 polarisation assay of CD4⁺ cells isolated from IR-P and rhCG in combination with IR-P3 treated NOD mice, while moderate inhibition was found in Th1 polarisation by rhCG and IR-P3 alone. This shows that in NOD mice treated with rhCG in combination with IR-P3 give massive inhibition of Th1 outgrowth. Which suggests that IR-P3 fraction needs rhCG for it maximal inhibition of Th1 subsets.

NOD/LTJ INVIVO TREATMENT (ANTI-CD3 STIMULATION)

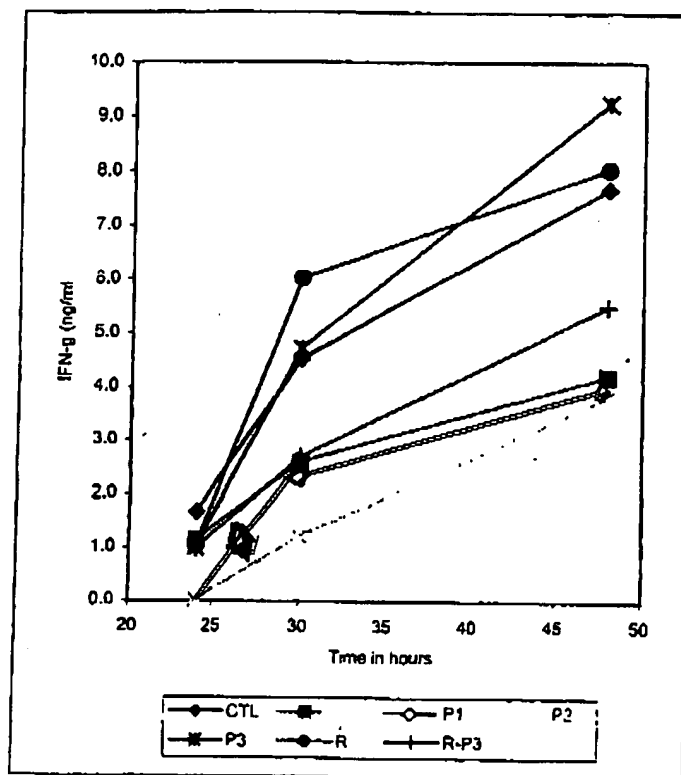


Figure 65

FOR MORE DETAILS, SEE DOCUMENT

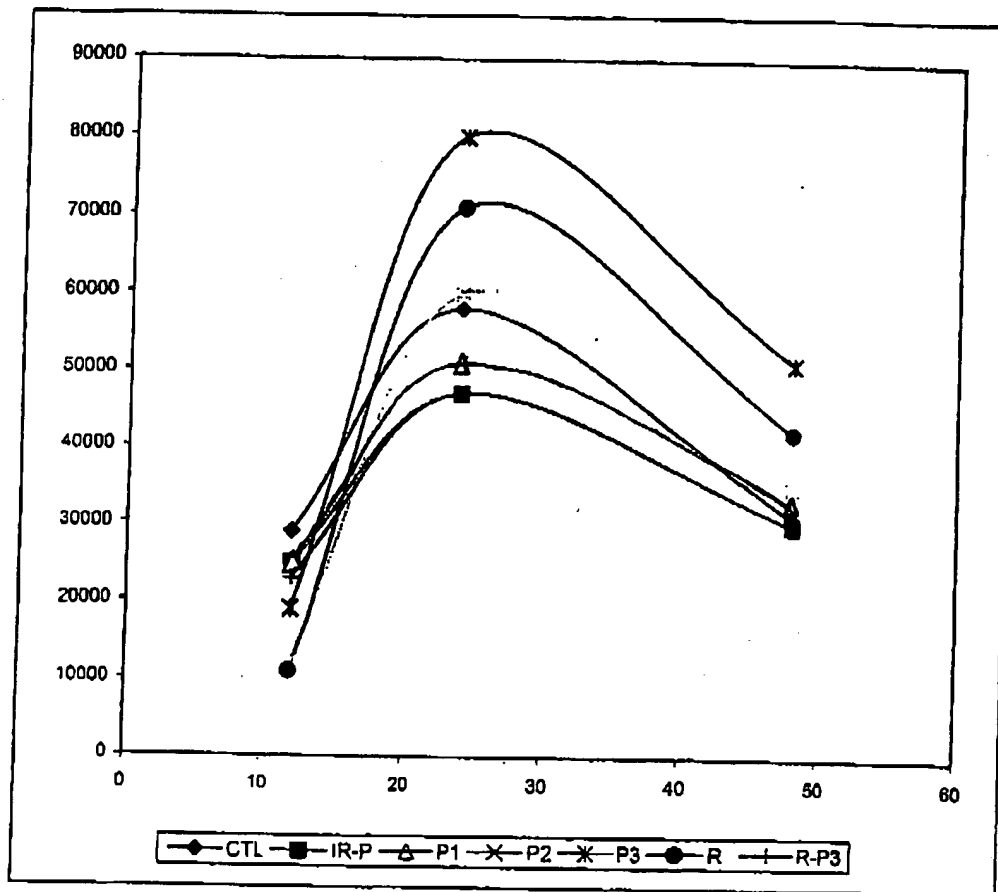


Figure 66

FOR MORE DETAILS, SEE DOCUMENT

09767-1100

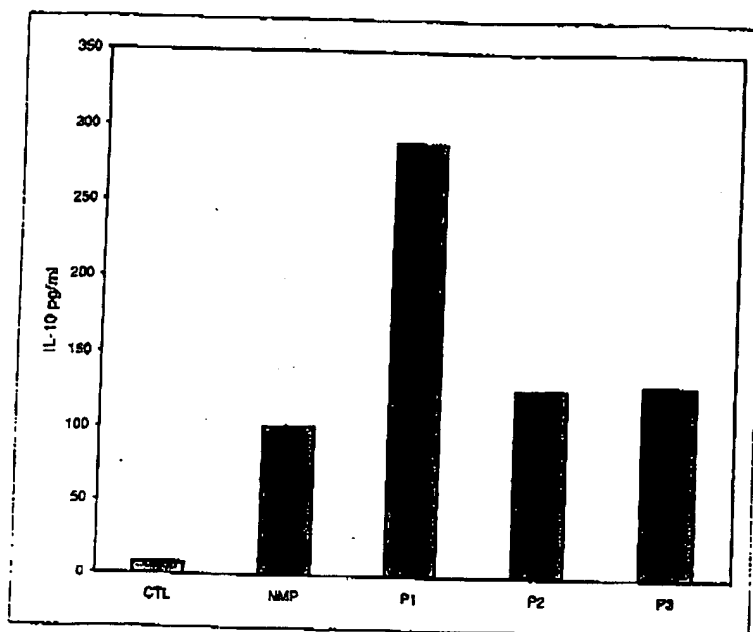


Figure 67 shows that IR-P and its fractions promote IL-10 production of anti-CD3 stimulated spleen cells from treated NOD mice as compare to PBS treated mice.

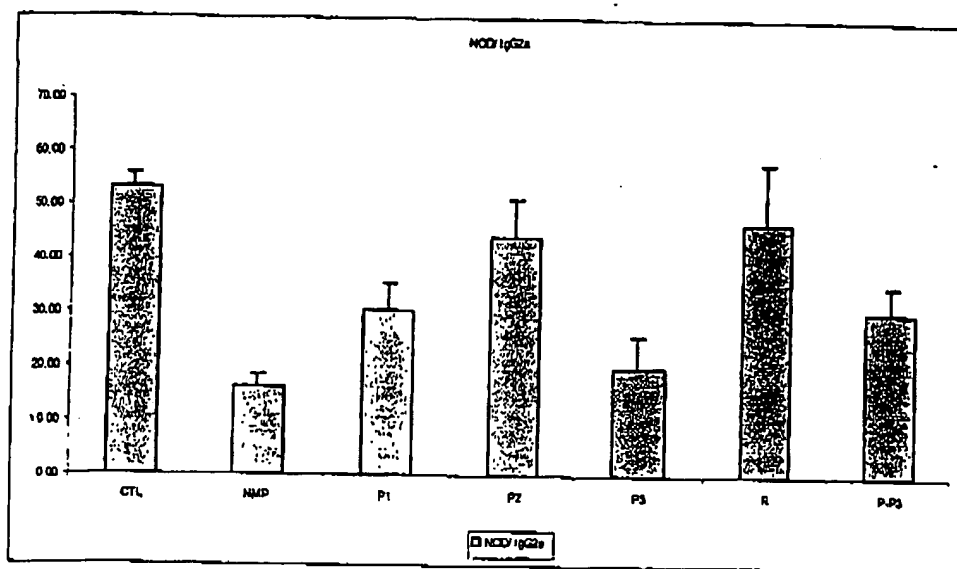


Figure 68 shows that IgG2a production is not inhibited by IR-P2 and rhCG in vivo treatment, while IR-P, IR-P1, IR-P3 and rhCG in combination with IR-P3 inhibit IgG2a production.

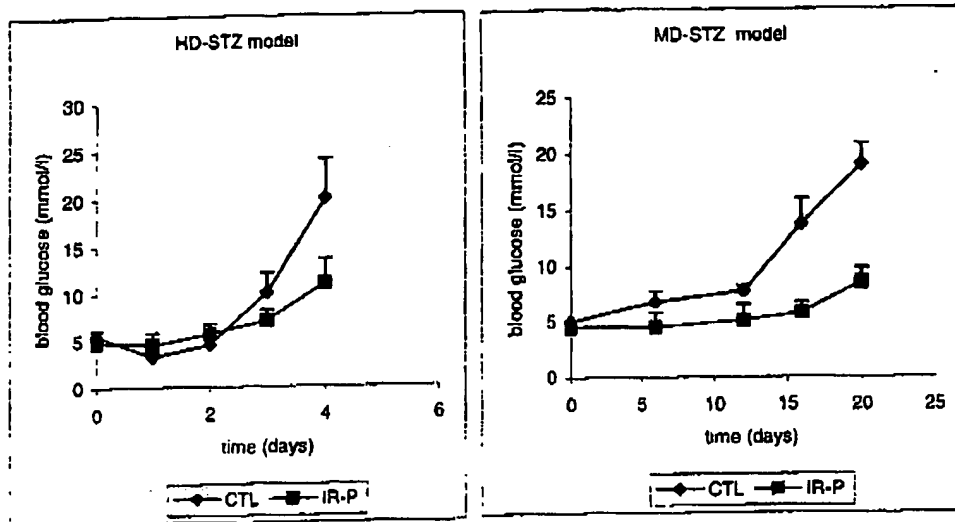


Figure 70

Figure 69

Figure 69 and 70 shows that IR-P treatment is able to delay the induction of diabetes in both model, HD-STZ as well as MD-STZ.

Figure 71

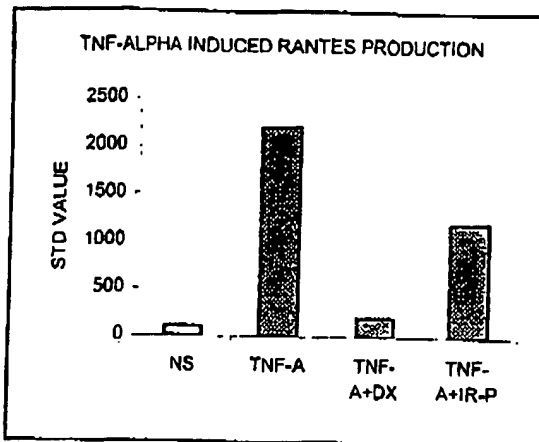


Figure 72

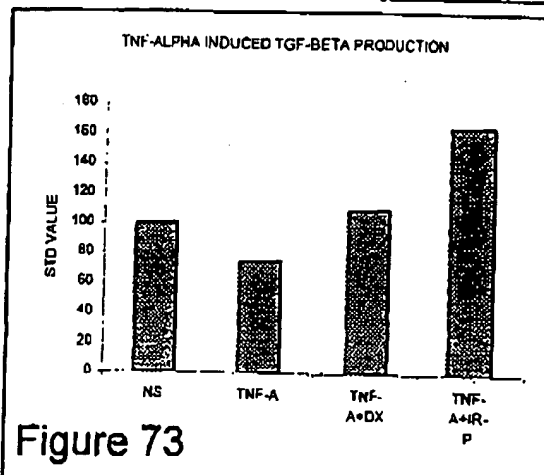
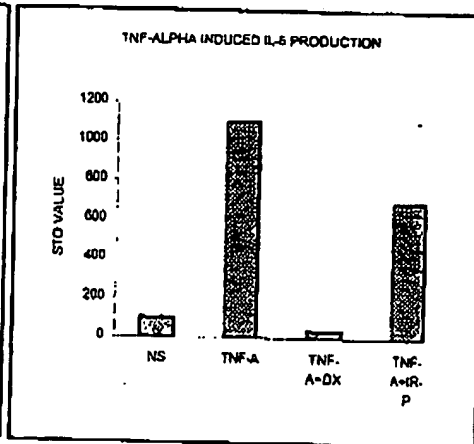


Figure 73

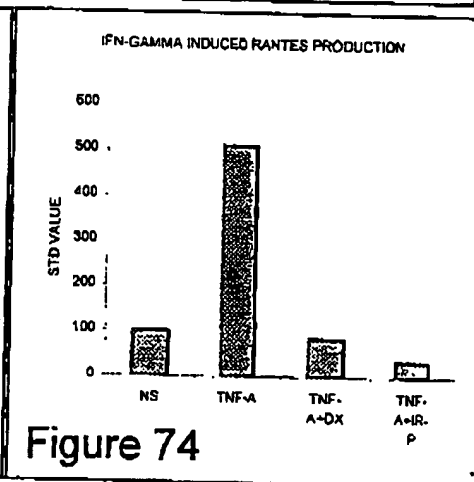


Figure 74

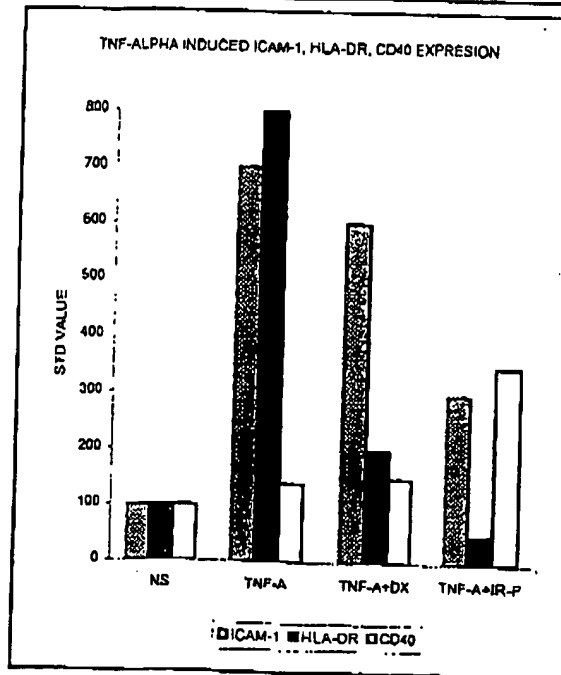


Figure 75

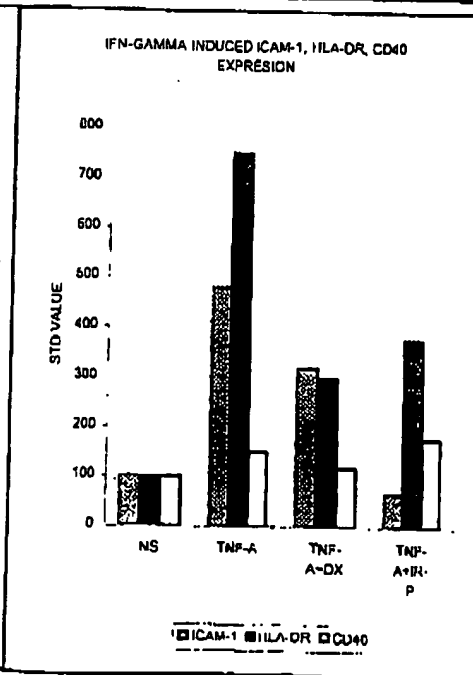


Figure 76

[illegible]

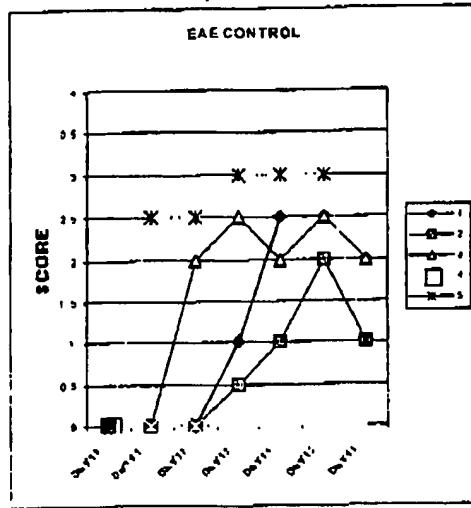


Figure 77

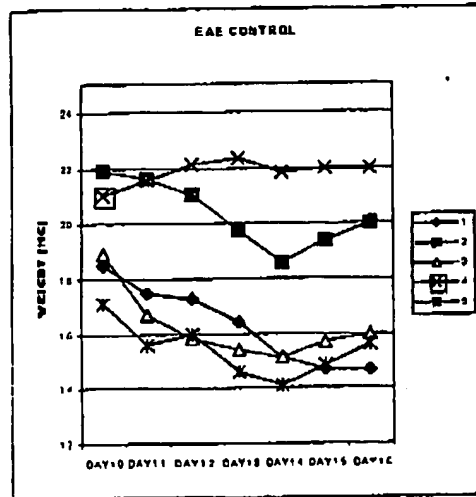


figure 78

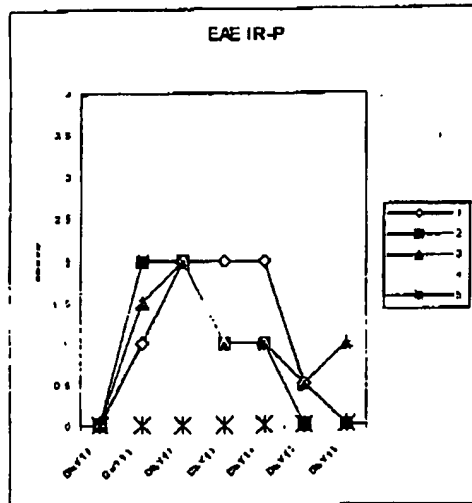


Figure 79

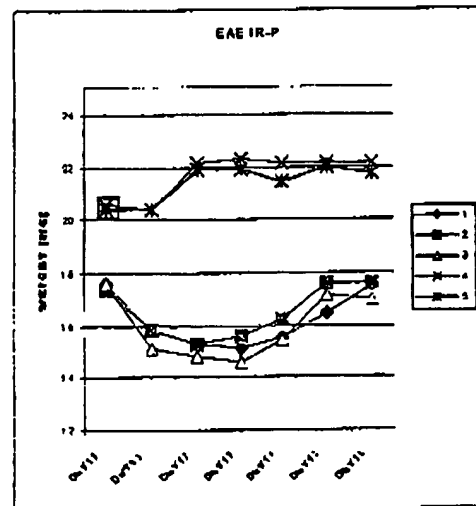
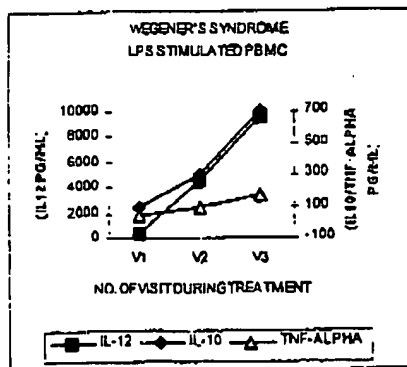


Figure 80

Figure 81

	Before Tx	during Tx	end Tx	Normal (X 10e9)
Lymphocytes	0.59	0.75	1.56	1.5 - 4.0
T cell	0.57	0.72	1.48	0.9 - 2.8
CD4	0.24	0.26	0.59	0.5 - 1.7
CD8	0.31	0.41	0.23	0.3 - 0.8
B-cell	0.01	0.01	0.01	0.1 - 0.3

Figure (82a)



(82b)

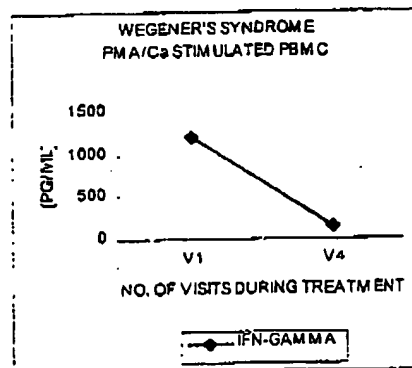


Figure 83

	Before Tx	during Tx	end Tx	Normal (X 10e9)
Lymphocytes	2.87	2.06	1.22	1.5 - 4.0
T cell	2.35	1.59	1.02	0.9 - 2.8
CD4	1.95	1.26	0.82	0.5 - 1.7
CD8	0.49	0.37	0.18	0.3 - 0.8
B-cell	0.33	0.19	0.14	0.1 - 0.3

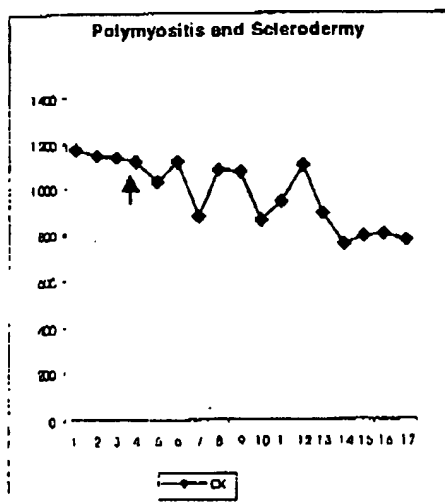


Figure 84

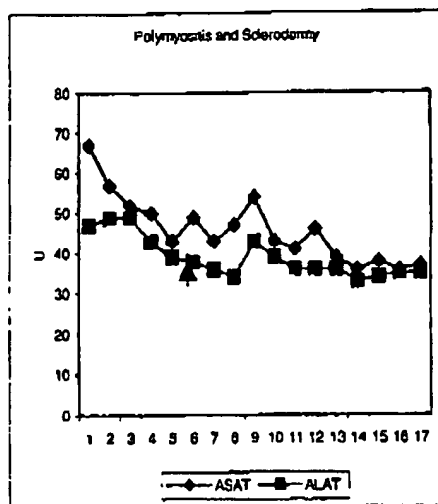


Figure 85

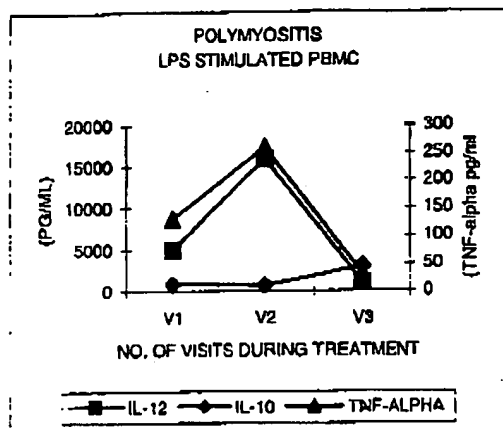


Figure 86

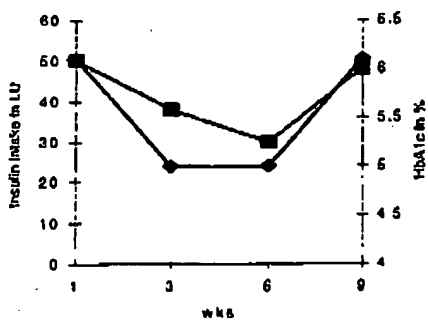


Figure 87

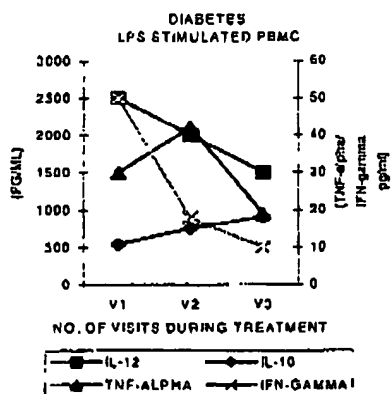


Figure 88

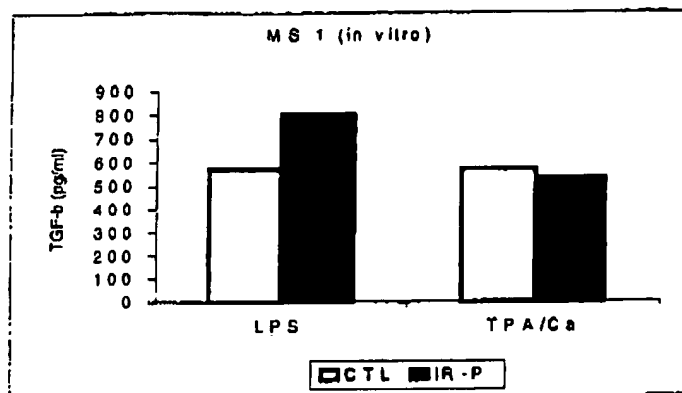


Figure 89

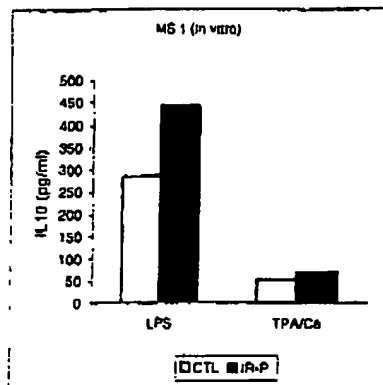


Figure 90

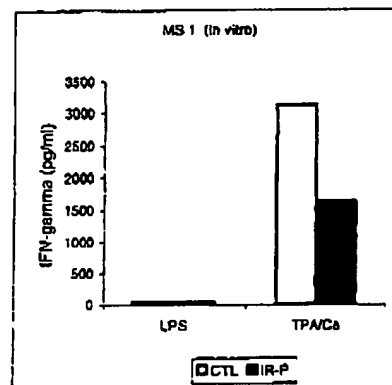


Figure 91

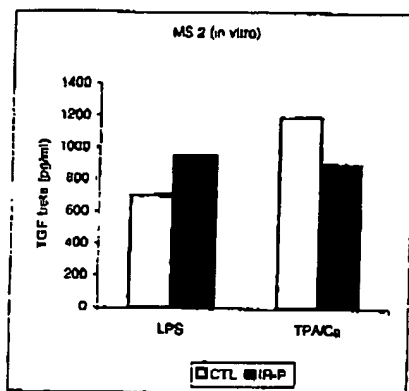


Figure 92

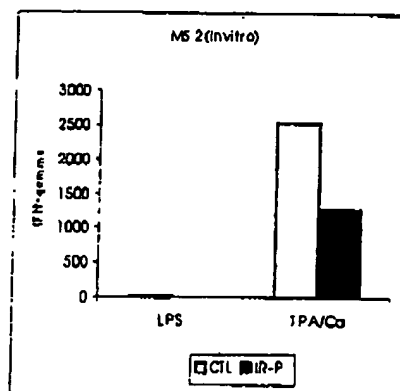


Figure 93

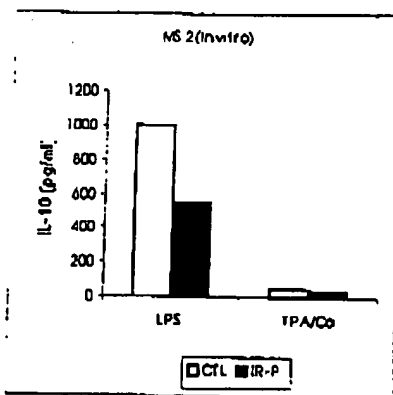


Figure 94



Figure 96

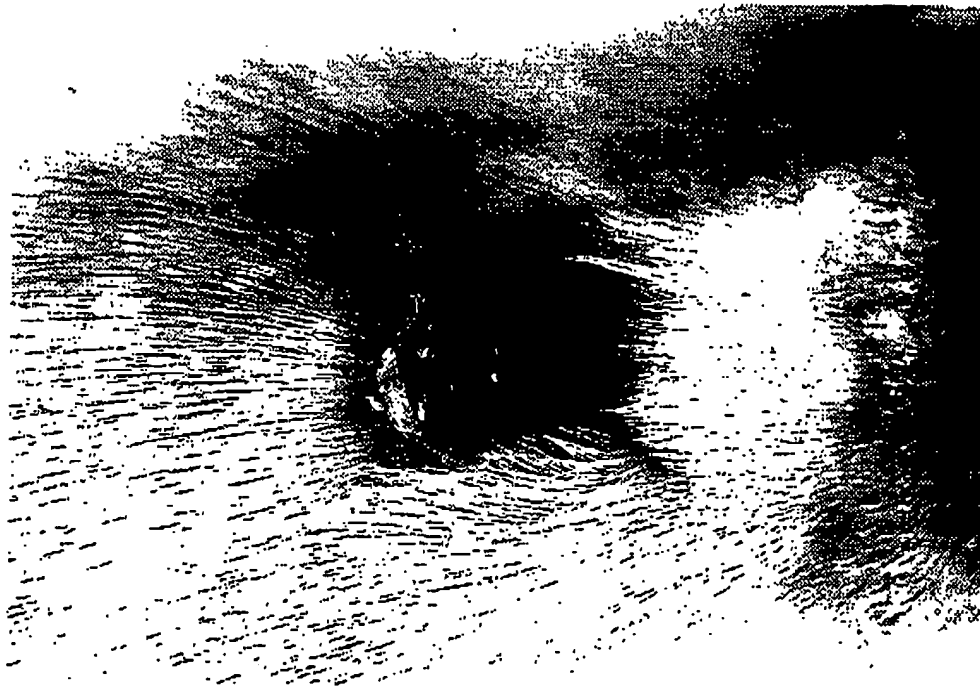


Figure 95

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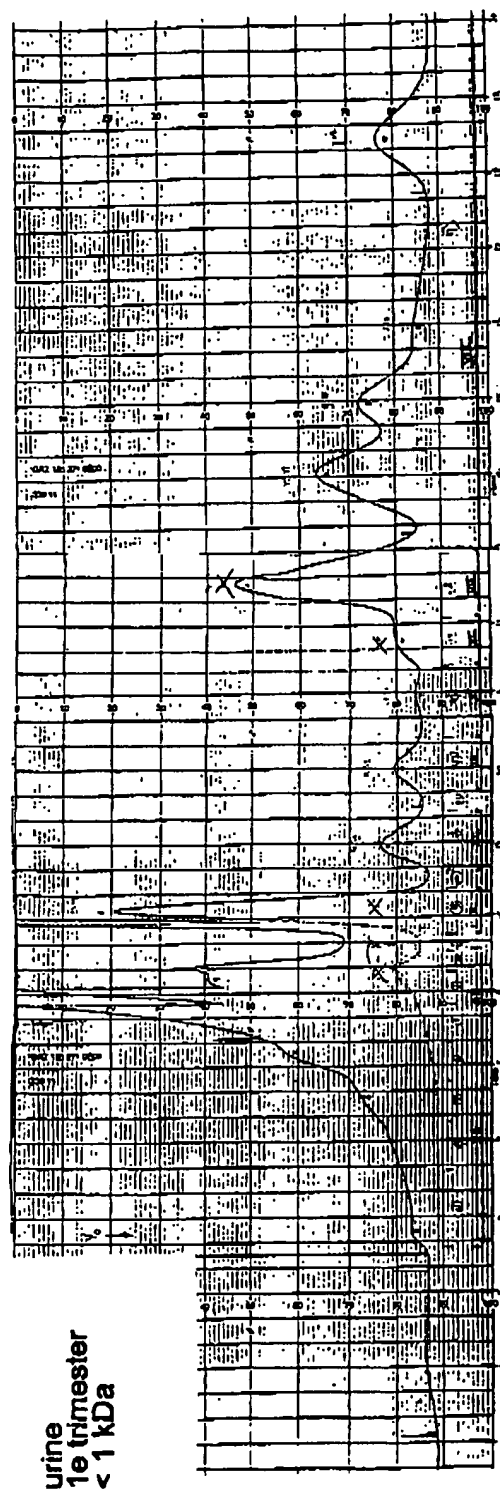


Figure 97

000217" 2/29T/60

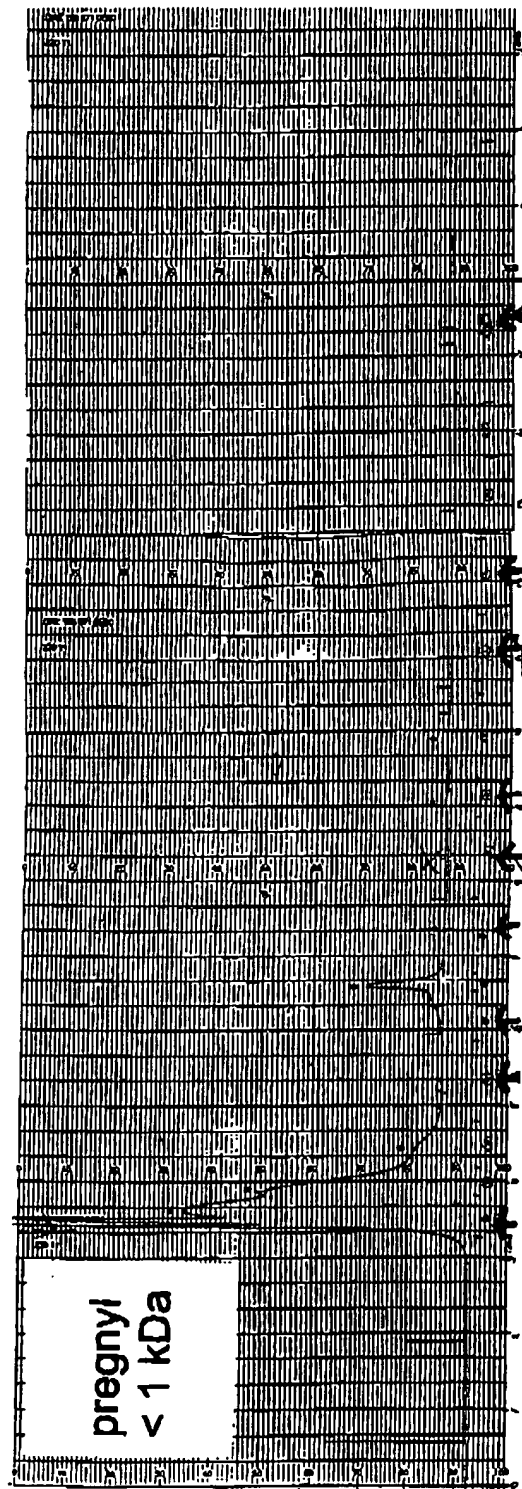


Figure 98

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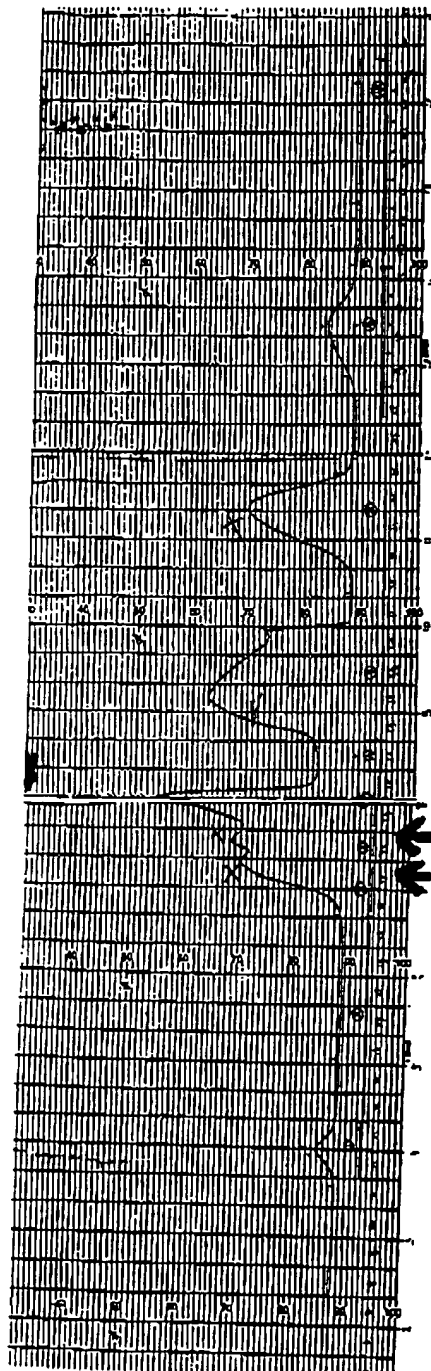


Figure 99

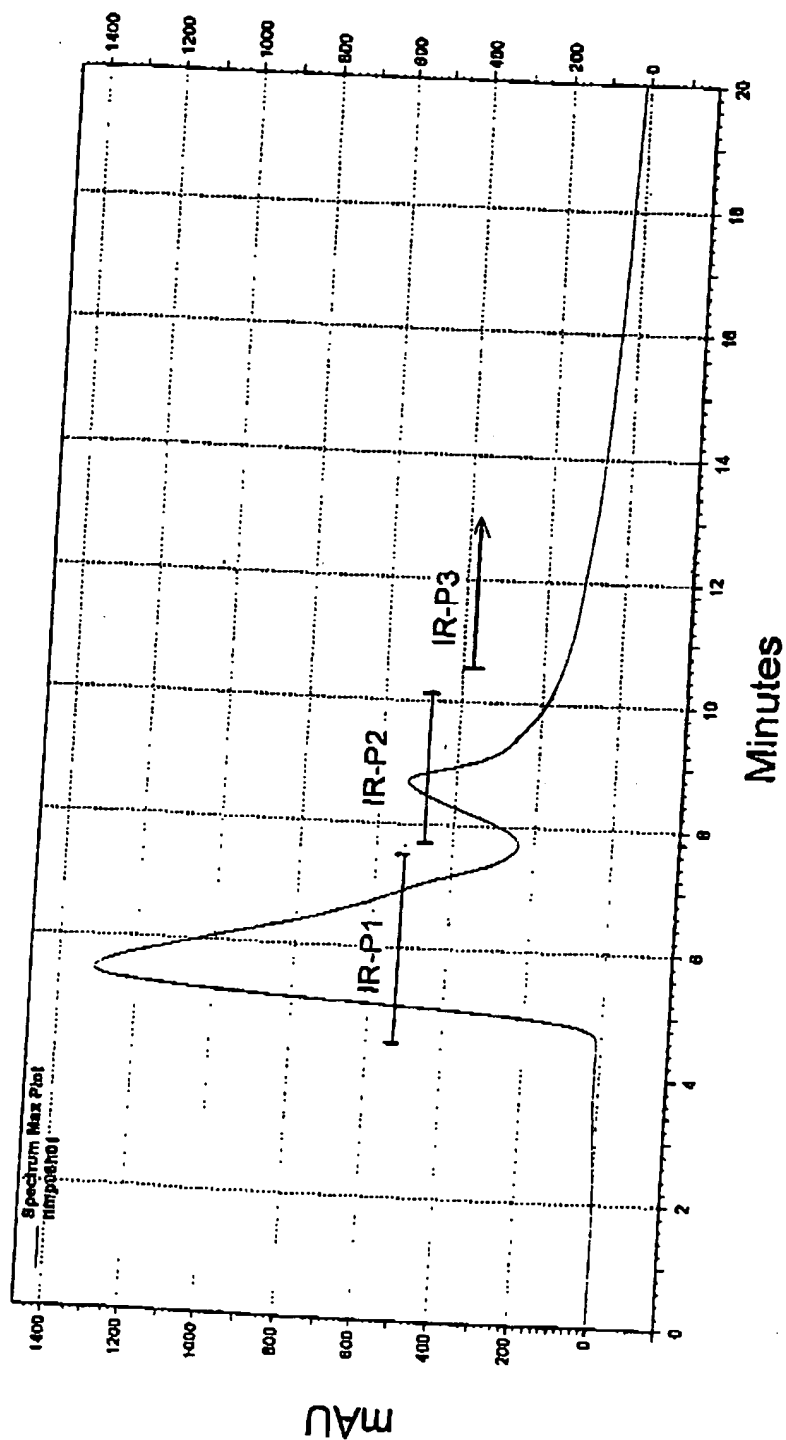
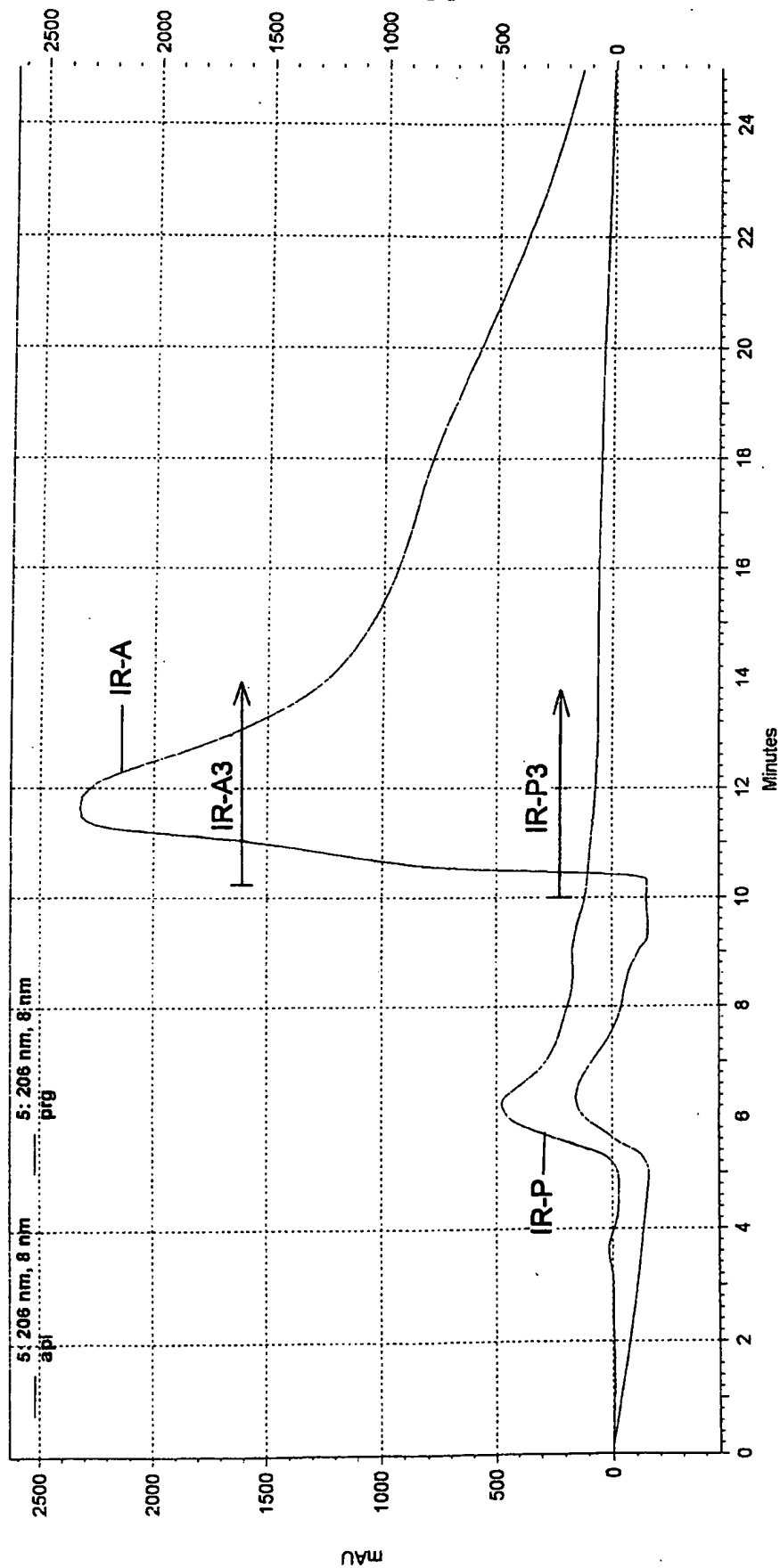


Figure 100



GPC 60 Å

Figure 101

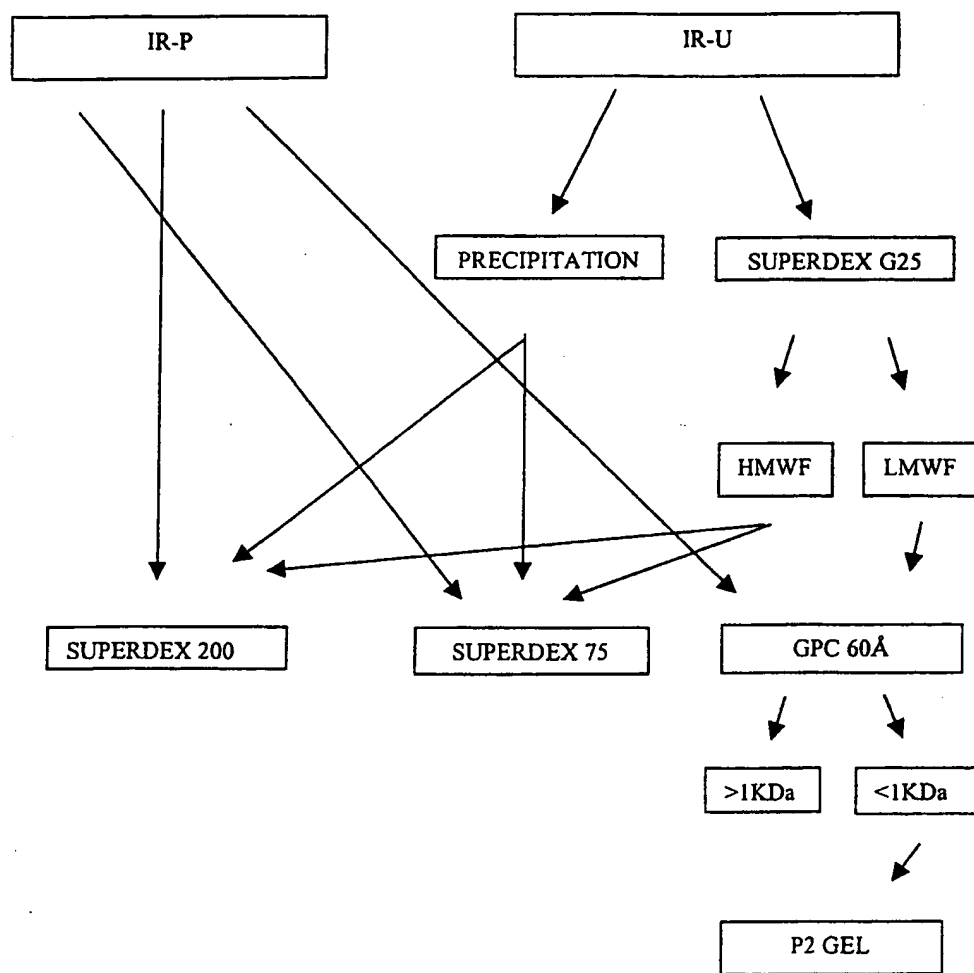


Figure 102